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Corticohypophyseal Obesity — Ignacio de Salcedo

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Corticohypophyseal Obesity*

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One of the problems that has always intensely interested investigators is the etiopathogenesis of obesity and, specifically, the possibility that the endocrine system is responsible for its genesis and development. At first, obesity was attributed to glandular changes, but before long it was denied that these changes were responsible.

In 1932, when Harvey Cushing described the first cases of pituitary basophilism, it seemed that the concept of endocrine obesity was justified, and some investigators, such as Rynearson and Gastineau,[1] who had opposed the theory that the endocrines play a role in the pathogenesis of obesity, admitted that Cushing's syndrome is, possibly, the only example of glandular obesity; yet, at the same time they quoted the opinion of Ingle:[2] "The importance of the adreno-cortical hormone in the production of this syndrome has not been adequately proved."

Within the group of obesity cases, is there not perhaps a percentage of patients who are obese because of endocrine changes? This was the question in our mind when, in 1950, we initiated the present work.

We must confess that in the beginning, we thought we would be dealing with more or less frank cases of Cushing's disease, although in a specialized clinic such as ours, we may have been inclined toward a too easy diagnosis of the syndrome. We had to revise all our data, with the result that of 14 previous diagnoses of Cushing's syndrome, only 1 patient was observed really to have the disease.

Consequently, it was a question of either admitting wider limits, modifying some of the classic fundamental concepts of Cushing's syndrome (this latter course did not seem reasonable to us in view of the unequivocal existence of sufficiently clear symptomatic pictures), or, more logically, continuing the study of the observations in the hope that we could find a satisfactory solution.

* This work is a summary of the thesis presented for fulfillment of the degree of Doctor of Medicine. The reader will find all details of the clinical and analytical data obtained, as well as an exhaustive bibliography, in the original complete text.[3]

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It is stated that excessive alimentation is the cause of obesity; while this is true in the majority of cases, it does not always apply.

In the large majority of cases, obesity is seen not only as a problem of esthetics but perhaps, consciously or unconsciously, it is compared to an excess of health, resistance, and security. To be fat is to be stronger, to possess more capacity for defense against biological aggressions, and as fat does not cause pain and a good appetite indicates health (because during illness a loss of appetite is normal), difficult and thankless becomes the task of the physician who attempts to change a condition that seems so salutary.

In reviewing the theories, whether past or present, that attempt to explain obesity, we find the predominant notion that the role played by the glands is insignificant and secondary.

This negation rests on weak premises, such as the original concept that ordinary obesity is due to glandular changes. In fact, an argument such as that of De Gennes,[4] which presupposes the irresponsibility of the gonads in the etiopathogenesis of some cases of obesity for the reason that it is impossible to correct these cases with sexual hormone treatment, seems unilateral. It is obvious that two weaknesses predominate in this assertion. In the first place, it is presupposed that obesity is due to some insufficiency, and on the other hand, the multiple possibilities of glandular intervention are ignored. It is quite certain that all obese patients are overweight, but we cannot deny the existence of various types whose pathogenic origins are different. The same is true of patients who are underweight. An individual may be underweight because he is tubercular, addisonian, diabetic, leukemic, or simply because genetic factors (for want of a better designation) determine that he should be so. The progressive increase in weight, due to additional fat (which is the basis for the definition of obesity), is merely a symptom common to diverse diseases.

We studied 44 patients, 25 of whom were female and 19 male (5:4 ratio); all but 2 were adults.

The average age of all patients examined was 29 years and 8 months, with an age range of 11 to 58 years. In more than half of the cases (25, or 57 per cent), the ages ranged from 20 to 40 years, in 11, between 11 and 20, and in 8, between 40 and 58 years.

Fourteen women (56 per cent) were, at the time of consultation, between 20 and 40 years of age, the general average being 28 years and 9 months, with a range of 13 to 49 years. In the 19 males observed (average age about the same as that of the females: 31), a more scattered age distribution was noted; 10 patients were between 20 and 40 years of age, 5 were more than 40, and the remaining 4 were between 11 and 20. The infrequency of this type of syndrome obliged us to consider it a rare eventuality, even for a specialized clinic, and very rare in the Department of Endocrinology of our Faculty of Medicine. In a total of 2147 patients examined up to August 1955, the syndrome was diagnosed 41 times (1.9 per cent). When the total obese cases were classified independently of any other factor, 7.5 per cent fell into this group, a percentage that increases to 15.7 per cent if one calculates the proportion in relation to the 260 obese plethoric patients examined.

The average weight of the patients was 95 7 Kg.; their median height was 1.592

meters. In 15 cases, the weight was 100 Kg. or more: 8 weighed more than 110 Kg., and 7, more than 120 Kg.; one of the patients weighed 147 Kg. The obesity is characterized by definite peculiarities, and is constant in its localization (fig. 1). In the face, which is described as a "moonface," the fat predominates in the temporal, genial, and masseteric regions; the over-all impression is that of a fat-cheeked face, but it is lively, and the dullness and droopiness that typify the heavy, sad expression of Cushing's syndrome are not present.

Adiposity is always seen in the inferior part of the cervical region. The presence of a "buffalo hump," which is rarely painful, was noted in 10 cases (22.7 per cent) — in 6 of the 25 women and in 4 of the 19 men.

Thoracic adiposity is accentuated predominantly in the superior half. Frequently, the retromammary localization resembles pseudogynecomastia.

As in Cushing's disease, the abdomen of the patients in all cases showed extraordinary subcutaneous adiposity, which resulted, even in the older patients, in accentuated tension and a protruding abdomen. In the 11 patients who had had unilateral adrenalectomy, we noted a conspicuous accumulation of previsceral fat.

Concerning the limbs, contrary to the tendency in Cushing's syndrome and notwithstanding a distribution of a rhizomelic predominance, we had no cases in which

FIG. 1. Thirty-three year old patient who became ill at 30 years of age. In three years he gained 46 Kg. Note the pronounced truncal obesity and the suprapubic striae. Death by cardiac infarct. No autopsy was performed.

the legs could be considered really thin, for there was no atrophy of muscular mass.

We found atrophic striae of the skin in all patients of both sexes. They were habitually localized in the pectoral regions (particularly in women), the deltoid and anterior axillar regions, the abdominal wall (preumbilical or inguinal), the hips, and, less frequently, the thighs.

In 24 women, the cutaneous striae had a more or less vivid pink coloration, which could hardly be described as purpuric or cyanotic, except in 1 case.

Similarly, 18 men presented striae of like degree, but it should be mentioned that 1 of them had a cyanotic stria and another had several striae of this kind. The striae occurred in 96 per cent of the women and in 95 per cent of the men.

All the women presented various degrees of hirsutism, accompanied in 15 cases by follicular hyperkeratosis. These hyperkeratotic lesions were observed in 15 of the 19 men. Android distribution of the pubic hair was noted in 24 women.

Clinical examination of the various systems revealed the following: (a) Digestive system: Except for a definite increase in appetite and thirst, no important changes were observed.

(b) Respiratory system: Clinical, radioscopic, and radiographic exploration did not show any findings of semeiological value.

(c) Circulatory system: In 19 women and in 15 men, dyspnea was observed, generally after light exertion; in 9 women and 12 men, palpitations frequently occurred and were independent of exercise or posture; malcolar or pretibial edema was present in 12 women and 9 men.

Taking, as normal maximum values, 150 mm. of mercury for the systolic pressure and 90 mm. for the diastolic, it was inferred that in the 44 cases observed, a total of 15 presented systolic hypertension (34 per cent), 15, diastolic hypertension, and 11, both types (25 per cent). In 11 cases the systolic pressure was equal to or more than 105 mm. of mercury.

The electrocardiogram of the patients both at rest and after exercise in 26 patients (14 females and 12 males) gave the following results: in 10, signs of alteration of the ventricular parietal conductibility; in 3, deviation of the electric axis to the left; in 4, sinus tachycardia; in 1, hypertrophy of the left ventricle with sinus arrhythmia; and in another, supraventricular extrasystolic arrhythmia. The exercise test was systematically normal.

(d) Nervous system: Twenty of the 25 women observed (80 per cent) and 10 of the 19 men (53 per cent) complained of headache, usually moderate, localized in the frontoparietal region, whose incidence we could not relate to any other symptomatology. Thirteen women and 7 men suffered from vertigo. Nine women and 7 men reported an increase of drowsiness in the daytime.

Although 1 woman and 5 men reported visual changes (amblyopia, diplopia, scotoma, etc.), we never found any alterations in the fundus, even in those patients showing definite radiological signs of pituitary adenoma. We never found ophthalmological signs of hypertensive retinopathy.

There were psychic changes in 18 of the 44 patients (40.9 per cent)—11 women and 7 men (44 and 37 per cent, respectively)—the reactions of a slightly depressive type being predominant.

(c) Urogenital system: In 2 patients, one of each sex, there were important renoureteral anomalies; in the woman, the descending urography indicated left renal aplasia; in the man, we observed bifid ureters. Colicky crises caused by renoureteral calculi occurred in 1 patient.

The urine showed a low *p*H value in all 32 samples tested. In the women, whose menarche began at the average age of 12 years and 2 months, various changes occurred; in 4 cases, the intermenstrual period lasted for more than 90 days, and in 4 others, there was a tendency for this duration to become progressively longer. In conjunction with this, it was observed that 60.8 per cent of the female patients showed menstrual changes, which were generally of an oligohypomenorrheic type.

In 7 men, there existed more or less complete impotence.

Studies carried out for the purpose of evaluating the possible participation of the internal secretory glands revealed findings whose value appeared to be indisputable.

Pituitary. In 12 of the 44 lateral roentgenograms of the skull carried out, we saw definite augmentation of the diameters of the sella turcica, 8 of which were obviously tumoral. In only 1 man was this tumoral condition observed.

From the hormonal point of view, only gonadotrophin estimation was carried out (follicle-stimulating hormone, adsorption in kaolin). In the women, we observed 9 low values (36 per cent), 4 normal, and 12 high (48 per cent). In the men, there was a general tendency toward low values; in 12 cases (63 per cent) the prolanurias did not reach 9 m.u./24 hours; in 5 they were normal, and in only 2 did we find high values.

Thyroid. Five women (20 per cent) presented a more or less obvious goiter of a diffuse colloid type. In 1 of these women, tubercular strumitis was histopathologically and bacteriologically confirmed. In 3 women and 3 men there was slight bilateral exophthalmos, a condition coexisting with goiter in the women.

Basal metabolism tests (Krögh's method) showed normal values in 17 women (68 per cent), below −11 in 2; the highest was +32 per cent. In the men, we observed normal values in 63 per cent, low in 15.7 per cent.

The estimation of total cholesterol (method of Bloor, Sobel, and Mayer) gave results higher than 2.5 Gm. in 8 women and 6 men, the highest value being 4.5 Gm./liter.

Parathyroids. The radiological aspect of the bones did not reveal any findings of diagnostic value. In all cases we carried out blood estimations of inorganic phosphorus, alkaline phosphatase (Bodansky), calcium (Ward), and the ionized fraction of calcium.

The variations as a whole had no special significance.

Adrenals. Our main interest was, naturally, to study possible adrenal changes; therefore, we carried out a large series of tests which, although not complete because of our limited facilities, were thought to be adequate for a reasonably certain diagnosis.

A pneumoretroperitoneum was carried out in all patients; we used the translumbar technique in the first 3 and the precoccygeal in the remaining 41. A bilateral hypertrophy was observed in 13 women (figs. 2 and 3), a left unilateral in 5, and a left adenoma in 1 (fig. 4), 52, 20, and 4 per cent respectively.

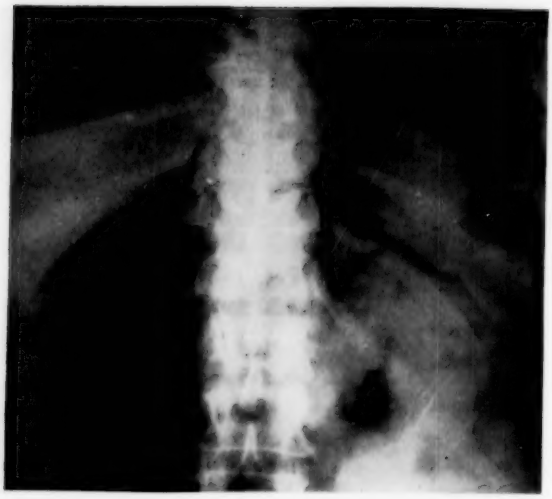

FIG. 2. Pneumoretroperitoneum in which two adrenals are moderately enlarged, verified surgically.

In the men, a bilateral hypertrophy was seen in 5 (26 per cent), a right unilateral in 1 (5 per cent), and a left unilateral in 6 (32 per cent).

11-Oxysteroids (Phosphomolybdic Ion). In 20 women (80 per cent), the values were

FIG. 3. Pneumoretroperitoneum showing pronounced bilateral hyperplasia of the adrenals, verified surgically.

normal, low in 1, and high in 3; in the men, they were normal in 13 (68 per cent), low in 3, and high in another 3 (15.8 per cent).

17-Ketosteroids (Callow). In 9 women the values were normal (36 per cent), 2 moderately low, 9 moderately high, and 7 (28 per cent) frankly high. In the men, where there was, habitually, a greater variation in the normal values, we found 15 cases (78.9 per cent) with normal and 4 (21 per cent) with high values.

Chromatography of the 17-Ketosteroids (Column of Aluminum Oxide, Dingmanse). The fractions II + III and VI + VII were frankly augmented, absolutely and relatively, in 97.3 per cent of the patients. The variations of the other fractions could not be considered significant.

Hydrocarbon Metabolism. We observed that the basal glycemia was within the normal limits (Kingsley-Reinhold-Fister) in 19 women (76 per cent), high in 5 (20 per cent), and frankly low in 1. Eight of the men (42 per cent) showed hyperglycemia during fasting.

Prediabetic curves, seen in 2 women and 7 men (8 and 36 per cent, respectively), showed the lack of a parallel between the basal glycemia and the subsequent development of the curve. One woman and 1 man presented diabetes mellitus.

Urea (Hypobromite). Estimations carried out on the 44 patients gave normal results in 21 women (84 per cent) and in 10 men (52.6 per cent); in no case did the values exceed 550 Gm.

Uric Acid (Brown and Herman's Method). In 76 per cent of the women and 84 per cent of the men, we noted severe uricemia.

Total Proteins (Biuret). Estimation in 23 women and 16 men showed moderate

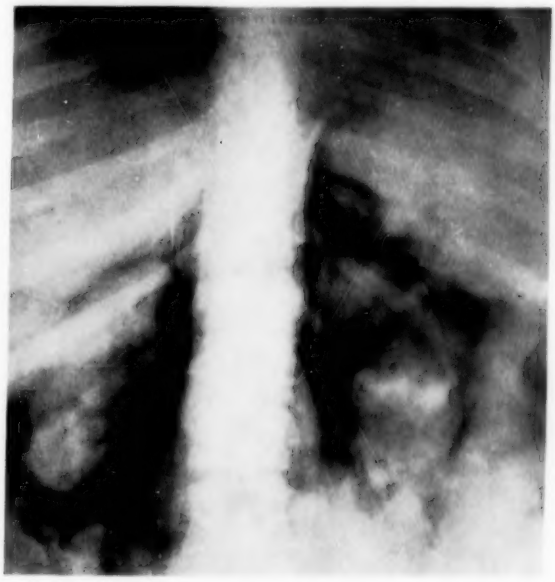

FIG. 4. Pneumoretroperitoneum showing a massive adenoma of the left adrenal, proved surgically.

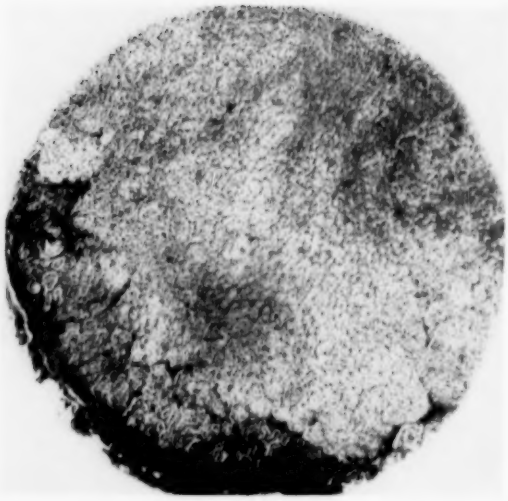

FIG. 5. Corticoadrenal hyperplasia, predominantly of the fasciculata. Hematoxylin-eosin (×24).

increase in 12 women (48 per cent) and 9 men. Electrophoretic fractionation on paper carried out in 34 cases indicated a diminution of albumin in 55.8 per cent of the patients and less marked variations in the remaining fractions.

FIG. 6. High magnification of another adrenal showing marked hyperplasia of the fascicular zone. Hematoxylin-eosin (×250).

Sodium (Flame Photometry). This was determined in 43 patients. Thirteen women and 9 men (52 and 47 per cent, respectively) showed normal values between 137 and 147 mEq./liter; in 4 women (16 per cent) and 4 men (21 per cent), the figures were somewhat high (up to 155 mEq., except in 1 woman with a reading of 162.3 mEq.). In the remainder, moderate decreases were observed.

The general mean of the results was entirely normal: 141 mEq./liter.

Potassium (Flame Photometry). Here, the variations were less marked, a slight diminution being observed in 3 women and in 2 men, and an increase in 1 man, taking as normal limits, 4.0 to 5.6 mEq./liter. The general mean was 4.44 mEq./liter.

Hemogram. The erythrocyte count was almost normal; in 7 patients (15.9 per cent) we observed leukocytosis (between 10,000 and 14,000).

The differential blood count showed neutropenia in 8, neutrophilia in 2, moderate eosinophilia in 7, lymphocytosis in 5, and lymphopenia in 1 patient.

Anatomicopathological Changes. As we performed no necropsies, the observations had to be limited to the histopathological study of adrenals removed from 11 other patients (7 women and 4 men) and the examination of the skin of 3 patients for atrophic striae. The investigations were carried out in the Department of Anatomic Pathology of the Faculty of Medicine.*

We observed only 1 case in which there were no histological changes of the gland. Examination of the remaining cases revealed a cortical adenoma in 1 patient, a predominantly adenomatoid cellular appearance in the zona fasciculata in 4, and diffuse hyperplasia in the 5 others (figs. 5 and 6).

Biopsy of the skin showed the epidermis to be verrucose, with foci of leukocytic hyperdiapedesis around several vessels of the dermis, and dissociation and rarefaction of the elastic fibers.

DISCUSSION

From the clinical and laboratory studies made in 44 patients (taking into account histopathological findings, as well as the evolution of the disease and therapeutic results), we concluded that there exist, in this group of patients, some endocrine alterations, particularly of the adrenal and hypophyseal types.

Morphologically, all patients showed various degrees of plethoric obesity of faciotruncal and rhizomelic distribution (similar to, but not the same as, that observed in Cushing's syndrome).

In the cases we studied, we noted a hyperproduction of 11-hydroxy-17-ketosteroids, and it can be stated that this excess acts in the same manner as in Cushing's syndrome. On the other hand, in view of the absolute difference in the muscular picture, as compared with Cushing's syndrome, we supposed that the normality of the androgenic functions counteracted the antianabolic effects of the other steroids.

Compared with common obesity, it was observed that the frequency of the symptoms or clinical signs was higher in patients in this series, and it seems to us that the

* By Dr. Amândio Tavares.

TABLE I

Frequency of Signs and Symptoms

Signs and symptoms	Cushing's syndrome		This series		Common obesity	
	Female, %	Male, %	Female, %	Male, %	Female, %	Male, %
Truncal obesity	80	83	100	100	8	24
Moonface	89	83	92	84	6	10
Buffalo hump	36	42	24	21	24	8
Purplish striae	72	75	4	10	0	0
Pink striae	0	0	96	95	2	0
Cutis marmorata	48	33	16	26	16	4
Acne	48	9	72	84	0	20
Bruises	36	9	16	5	0	0
Telangiectasia	?	?	68	84	2	18
Varices	?	?	8	5	26	2
Hirsutism	79		100		4	
Android pubic hair	27		96		2	
Hyperkeratosis (follicular)	?	?	60	79	34	2
Amenorrhea	64		8		1	
Impotence		75		37		2
Headache	36	33	80	53	30	10
Asthenia	48	33	60	58	4	22
Muscular atrophy	48	32	0	0	0	0
Hypertension, systolic	71	46	32	37	18	22
Hypertension, diastolic	84	81	28	20	9	12
Hypertension, mixed	92	92	24	26	9	22
Osteoporosis, in general	64	75	0	0	1	0
Osteoporosis of the skull	?	?	8	5	0	0
Fractures	20	0	0	5	0	0
Renal calculi	0	17	0	5	4	2
Hyperostosis frontalis interna	?	?	28	0	6	0, 3
Sella turcica augmented	4		40	10	2	0
Personality changes	24	33	44	37	0	0
Gynecomastia		?		26		0
Diabetes mellitus	26	33	4	5	11	6
Glycosuria	34		4	5	11	6
Glucose tolerance (prediabetic)	79		8	37	2	0
Fasting hyperglycemia	30		28	42	6	4
Urinary alkalosis	Frequent		0	0	0	1
Goiter	15		20	0	0	0
Exophthalmos	28		12	16	0	0
Serum sodium, normal	42		54	47	89	100
Serum sodium, +	33		17	21	11	0
Serum sodium, −	3		29	31	0	0
Serum potassium, normal	27		88	75	100	100
Serum potassium, +	15		0	5	0	0
Serum potassium, −	6		12	10	0	0
Cholesterol, total	78		32	31	50	43
17-Ketosteroids, normal	Often		36	78	81	80
17-Ketosteroids, +	40		28	21	4	20

Table I Continued on page 261

TABLE I (*Continued*)

Frequency of Signs and Symptoms

Signs and symptoms	Cushing's syndrome		This series		Common obesity	
	Female, %	Male, %	Female, %	Male, %	Female, %	Male, %
17-Ketosteroids, —	In adenomas		Sometimes		15	0
11-Oxysteroids augmented	80		13	16	Never	
Follicle-stimulating hormone, normal	Often		16	26	62	50
Follicle-stimulating hormone, +	Rarely		56	11	38	10
Follicle-stimulating hormone, —	Often		36	60	0	40
Red cells augmented	?		0	0	0	0
White cells augmented	43		19		0	0
Eosinopenia	Always		0		0	0

patients fell into an intermediate category. Although the groups were manifestly small, these results are still significant (table I).

The great frequency with which the increase in volume of the sella turcica was observed led to the clinical conclusion that there is a basophilic type of hyperfunction of the pituitary in the development of this syndrome.

The therapeutic results obtained by means of hypophyseal irradiation represent an important argument in favor of this interpretation.

Just as in Cushing's syndrome, it is possible that, prior to the participation by the hypophysis, other structures may play a role, especially the hypothalamus. We cannot ignore the possibility that obesity may be the primary cause of hypercorticalism, the adipose surcharge being a stress to which the organism would react, bringing into play the reactionary mechanisms that characterize the general adaptation syndrome. Yet, serious reservations are opposed to this attempt of simplification, since the majority of obese cases that we studied do not offer the same laboratory and clinical phenomena.

SUMMARY

From the clinical, radiological, and laboratory study of 44 patients (25 women and 19 men) belonging to the plethoric obese group and whom some authors would describe as suffering from Cushing's syndrome, the following conclusions are drawn.

In the group of the so-called plethoric obese patients, a minority have a clinical and laboratory symptomatology of corticoadrenal metabolic hyperfunction. However, they cannot be said to be suffering from Cushing's syndrome because of some fundamental differences. Moreover, their symptomatology did not change to that of Cushing's syndrome during the observation period, which extended to more than five years in some of our patients.

The histological examination of the adrenal glands removed in 11 cases confirmed this clinical and laboratory diagnosis and revealed, in all except 1 case, alterations of the fascicular and, less frequently, of the reticular zone.

Chromatographic fractionation of 17-ketosteroids in 37 cases, as well as the gland

morphology and metabolic alterations, showed a corticoadrenal hyperfunction to be the pathogenesis of this syndrome.

In about half the cases, the findings supplied by roentgenogram of the skull support the hypothesis of a pituitary involvement, which, clinically, would have to be basophilic.

The etiopathogenic factors of this syndrome would, therefore, be those currently accepted for Cushing's syndrome, differing only by their minor intensity and by greater virilizing corticoadrenal alterations. The comparative lack of severity of this syndrome would be due to the relative equilibrium of antianabolic action of 11-hydroxy-17-ketosteroids, which results from the normal or sometimes exaggerated production of corticoadrenal androgens.

In the patients submitted to surgery, the immediate and long-term results were frankly satisfactory. In patients who do not undergo surgical intervention, the evolution is unfavorable as a rule: an essentially chronic disease and cardiovascular and metabolic complications (imbalance of hydrocarbons in particular) are to be feared.

ACKNOWLEDGMENT

The author wishes to express his gratitude for the invaluable aid given by the professors of the Faculty of Medicine, Oporto, in particular, Drs. Amândio Tavares, Ernesto de Morais, Fernando Magano, Álvaro Rodrigues, and Joaquim Bastos. The author wishes to acknowledge the financial aid of the Instituto de Alta Cultura, under whose auspices this work was accomplished.

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Drug Sales Boom

Drug sales during 1957 reached a record high of more than $1.7 billion, according to a spokesman for the pharmaceutical industry. This represents an increase of almost 15 per cent over the previous year and is nearly double the figure for 10 years. Ethical drugs, dispensed only on prescription, comprise an estimated 65 per cent of the total expenditure for drugs in this country.

Value of Intravenous Amobarbital Sodium in Psychosomatic Disorders: An Access to Psychosomatic Management

Neglect of Its Use in Internal Medicine

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The need for proper management of psychosomatic disorders is greater today than ever before. With the ever-increasing stress of modern living and the unrest of our troubled times, emotional disturbances continue to increase in frequency and severity. Recent surveys have shown that at least 50 per cent of all patients seen in general or internal medicine are psychosomatically afflicted. And since most of those organically ill have added psychic difficulties, the figure of 75 per cent is probably closer to the actual incidence.

While the emotional disturbances are not lethal in the same manner as cancer and degenerative heart disease, still they are far more destructive in their general and vast disabling effect. Millions suffer from anxiety and related emotional disturbances. And this in face of the fact that there are only a few thousand psychiatrists in private practice, many of whom are out of financial reach of the great masses of patients; there are practically none in the rural areas.

With these large numbers of patients with psychosomatic disorders facing him daily, the internist—outside of nonspecific therapy such as oral sedatives, analgesics, vitamins, and hormones and prolonged supportive psychotherapy—has almost no specific and direct approach to psychosomatic diagnosis and therapy. And present-day psychotherapy is too ambiguously defined, is multischooled and multidivergent in its methods and goals, difficult in its practice, time-consuming, and too often futile. The internist is sorely in need of more specific and easily applicable methods of effective psychosomatic therapy.

The etiology of disturbed emotional states still remains generally obscure (in spite of the claims of the various psychoanalytical and psychotherapeutic schools), and treatment is as yet inexact, polymorphic, and far from the desired goal. But still, narcoanalysis and narcotherapy with intravenous amobarbital sodium (Amytal sodium*) are at present a diagnostic and therapeutic tool of relatively great value and very useful procedures in psychosomatic medicine, but surprisingly they are rarely used by the internist.

This paper will show that narcoanalysis and narcotherapy are ideally suited for the physician in internal medicine and should and can be used by him with great advantage in psychosomatic diagnosis and therapy. The author has successfully

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* The trade name of Eli Lilly & Co. for amobarbital sodium is Amytal sodium.

used amobarbital sodium in his practice of internal medicine, having given 12,154 injections in 1532 patients.

EMOTIONAL AND MENTAL EFFECTS

Bleckwenn[1, 2] was the first, in 1930, to report on the value of intravenous amobarbital sodium in emotional and mental disorders. He was able to produce a prompt and controlled narcosis or hypnosis. With the former, he found that he could quickly allay anxiety and disturbed mental states. With the latter, he perceived that he could easily reach levels of consciousness not ordinarily accessible. Other early investigators were Lorenz,[3] Solomon and co-workers,[4] and Lindemann.[5] Horsley[6] in 1936 originated the term "narcoanalysis."

World War II added impetus to the use of amobarbital sodium when Sargant[7] found it of immeasurable usefulness in the treatment of the psychiatric casualties of the Dunkirk evacuation, and when Grinker and Spiegel[8] reported on its specific psychotherapeutic dynamics in the combat stress of the North African campaign.

Since the work of these men, there has accumulated in the literature a sizable volume of reports by psychiatrists on amobarbital and thiopental narcoanalysis and narcotherapy, but no attempt will be made here to review these studies. This paper will present the author's 10 years of experience as an internist and will thus serve as an introduction to other internists who may wish to pursue further studies both in the literature and in their practice.

When injected intravenously, amobarbital sodium has the following effects: It relieves anxiety and depression; clears the thought content, re-establishes coherency and relevancy of expression, generates insight; induces free, spontaneous, uninhibited, and unrestrained verbal expression; facilitates ventilation and catharsis; lessens or abolishes the restraints of social conventions and standard morality; lessens or abolishes conscious or unconscious blockades, as in malingering and hysteria; brings to the surface the underlying and hidden true existing emotional state and trend of thought; creates desire in the patient for rapport with the therapist; produces a true hypnotic state.

DIAGNOSTIC USES

Diagnostically, intravenous amobarbital sodium serves as a short cut to the unconscious and effects a controlled hypnosis for the study of the inner mind. It has the following diagnostic uses.

It is a prodigious saver of time. All patients given the drug become overpowered with the desire to talk. Verbal expression flows freely and incautiously. Cultural and ethical barriers are temporarily removed. Suppressed situational material is dramatically revealed in a few moments, instead of in hours and weeks of questioning, for example, marital or employment difficulties, family strife, social maladjustments, conflicts, insecurity, frustration, envy, unrealized goals, sexual difficulties, environmental stress.

The drug brings to the surface the consciously or unconsciously concealed true state of emotions. It is an indicator of underlying illness, provides access to levels

of consciousness usually repressed, reveals trend of thought, and establishes contact with suspicious, seclusive, and inaccessible patients. It reveals anxiety, depression, or both in varying degrees; panic states: obsessive-compulsive thinking; covert or hidden fears of death, cancer, ill health, insanity; excessive worry; painful memories; self-condemnation; suicidal tendencies; obsessive guilt; disabling dependency; hostility; aggression; delusional thinking; paranoia; hallucinations.

The drug is very effective in unmasking hysterical or malingering manifestations, such as simulated paralysis, hysterical aphonia, functional blindness, psychogenic amnesia, malingering of somatic pain.

The drug aids in the diagnosis of doubtful or borderline psychotic states. The true psychotic state is revealed under amobarbital sodium, and psychotic trends are brought to the surface.

The drug is valuable as a screening method and prognostic aid in therapy. Patients who do not respond to amobarbital sodium indicate having deep-seated anxieties or emotional disturbances that require more involved psychiatric care, such as depth analysis or convulsive therapy. The need for electroshock is indicated in those depressions that do not respond to amobarbital sodium.

No special skill in analytical or hypnotic technique is needed. Continued use of amobarbital sodium in his practice will acquaint the internist with a usable technique of psychosomatic diagnosis and evaluation of the emotionally disturbed patient.

THERAPEUTIC USES

The therapeutic importance of intravenous amobarbital sodium, although stressed in the early reports, has been neglected in the recent literature and is not too generally appreciated. Many think the drug is of value only in narcoanalysis or diagnosis. Others are of the opinion that, like oral barbiturates, it has only a transient sedative effect. But intravenous amobarbital sodium has a specific and distinctive potency in allaying anxiety and associated disturbances quite different from that of orally administered preparations. One is afforded a brief glimpse into the unknown mechanisms of this therapeutic power when catatonics and withdrawn schizophrenics are transformed into completely lucid (albeit temporary) intervals after the injection of amobarbital sodium.

The hypnotic effect produced by intravenous amobarbital sodium has also been too often considered to have value only in diagnosis. But, as will be described here, it is equally effective in therapy. The following therapeutic uses can be listed.

Rapport with the patient is easily and more rapidly achieved. Patients become friendly and emotionally warm. Insight by the patient is readily acquired, and understanding is brought into his thinking and behavior, symptom causality, obsessions and phobias, hostility and aggression, guilt and fears. The troubled mind is unburdened by catharsis, ventilation, release of pent-up emotions. A controlled hypnotic state is produced in which the patient becomes amenable to suggestive therapy; reassurance and persuasion is more readily accepted; counseling, explanation, and guidance are facilitated.

The drug is useful in anxiety and depressive states. It relaxes tension, produces calmness, eases anxiety; produces increased feelings of well-being and serenity, mild euphoria, relieves depression; stabilizes the emotions; abolishes clouded and confused thinking; lessens and abates the somatic symptoms of anxiety. The drug is useful in relieving anxiety manifestations of general nervousness, uneasiness, constant distress, restlessness, feelings of panic, irritability, shakiness, insomnia, excessive and chronic worry, inability to concentrate, impaired mentation, emotional excitability, vague and indefinite apprehension, pessimistic and fearful anticipations. It is unexcelled for the relief of acute anxiety, acute panic, anxiety crisis of either endogenous or reactive (situational) origin, and it breaks the cycle of persistent insomnia.

Amobarbital sodium aids in the alleviation of depression: depression secondary to anxiety (reactive); and depression due to environmental stress (situational, reactive), such as melancholia, listlessness, inertia, crying spells, mood swings, absence of any optimism in thinking or feeling, suicidal tendencies, uncontrollable and prolonged grief. The drug assists in the relief of somatic symptoms of psychogenic origin such as vertigo; anxiety-tension headaches; functional fatigue; nonorganic pain in the face, head, extremities; tightness of the throat; neurocirculatory asthenia; functional chest pain; functional gastrointestinal disturbances such as abdominal pain, indigestion, gas, belching, spastic colon syndrome; nervous urinary frequency; tension backache; emotional hypertension.

The drug relieves the anxiety-depression components of any organic illness, such as angina pectoris, bronchial asthma, peptic ulcer, cancer, ulcerative colitis, essential hypertension; and it is valuable in war combat mental disorders, such as war anxiety or neurosis, recovery of forgotten or painful battle experience, reliving of emotionally traumatic episodes.

Amobarbital sodium is helpful in the treatment of such aberrant emotional attitudes and responses as hostility, aggression, obsessive thinking, fears and phobias, dependency, feelings of inferiority, guilt, paranoid trends. It provides strikingly effective therapy for the relief of hysterical or simulated paralysis, psychogenic aphonia, blindness, or amnesia; and it is of benefit in relieving the anxiety or depressive components of acute or chronic alcoholism.

An excellent and controlled sedative effect is achieved in toxemic delirium and exhaustion, postoperative excitement or anxiety, restlessness, and agitation of acute central nervous system disorders. The drug controls the convulsions of tetanus, strychnine, eclampsia, cerebral vascular accidents, status epilepticus.

METHOD

Dosage and Technique. Ampoules containing 3¾ and 7½ grains of amobarbital sodium are dissolved in 5 or 10 ml. of distilled water to make a 5 or 10 per cent solution. The 5 per cent, or even the 2½ per cent solution, should be given to those who (a) are easily narcotized, (b) are debilitated or ill with organic disease, and (c) have sensitive veins that are likely to become thrombosed or painful. Solutions that are not clear and solutions more than three hours old should be discarded. The

rate of injection is never to exceed 1 ml./minute. Actually, ½ ml. or less per minute produces better results in both diagnosis and therapy. The amount of drug is never to exceed 7½ grains in one injection. Larger doses, e.g., 15 grains, are used by others, but in the author's experience are neither necessary nor desirable for analysis or therapy. Also, limitation of the dose to 7½ grains excludes any possibility of prolonged narcosis, breathing difficulties, or circulatory collapse, and reduces the need for postinjection care of the patient.

Postinjection Management. Even with the maximum dose of 7½ grains, patients rarely need watching after injection. Patients usually sleep from 15 minutes to 1½ hours, depending on the amount of drug given and whether or not they are awakened. With the maximum of 7½ grains, any patient can be awakened at any time and, with assistance, can be rendered ambulatory if need be. After spontaneous awakening, no urging or assistance is needed by the patient to get up and walk. The great majority of patients are able to get home unassisted, either by driving their own cars or by other transportation.

THE AMOBARBITAL INTERVIEW: NARCOANALYSIS

The examination is carried out in a quiet, semidarkened room. No previous preparation, such as an empty stomach, is required. The patient is reassuringly told that he will receive an injection that will relax him and make him slightly drowsy.

A solution containing 7½ grains of amobarbital sodium dissolved in 10 ml. of distilled water is given intravenously at the rate of ½ ml./minute until the patient is relaxed and slightly euphoric, but fully awake. The injection is then stopped with the needle left in the vein, and questioning and discussion are begun. At this point, those using the technique for the first time are amazed at the rapid obtaining and intensification of rapport with the patient. Catharsis and ventilation of suppressed material proceeds with unbelievable absence of restraint. Delusions and hallucinations, if present, are revealed. Suggestion and interpretation by the analyst are readily and firmly accepted.

When the amobarbital seems to be wearing off, more is given until the state of optimal light narcosis is again reached, and questioning is resumed. This is repeated until sufficient information is obtained or 7½ grains has been given.

In the acutely tense patient in whom 7½ grains is not enough for hypnosis, subsequent injection interviews will produce the desired ventilation and catharsis. Some patients will reveal suppressed material after as little as 2 grains, while others, less frequently, may require two or three sessions of 7½ grain injections for full psychosomatic evaluation.

PROCEDURE IN THERAPY: NARCOTHERAPY

Small doses of intravenous amobarbital sodium produce calmness and diminution of psychic tension without clouding of consciousness. Moderate doses induce drowsiness. Large doses produce sleep.

Frequency of injection depends on the duration of illness, degree of underlying anxiety, and the severity of the somatic symptoms. Frequency may vary from once

daily in acute anxiety to two or three times weekly in moderate anxiety. Hospitalized patients with acute anxiety or agitation can be given two or three injections in 24 hours. In the usual moderate case, three injections weekly are given for three weeks, then two weekly for four weeks, and one weekly for five weeks—for a total of 21. Some patients need only three or six injections, whereas others have received as many as 40 injections.

The amount given in one injection varies in the same manner as frequency of injection. Severe anxieties usually require 7½ grains; moderate anxiety, 3¾ grains and even as little as 2 grains. But this is not a hard and fast rule. Some patients with severe anxieties do best on smaller doses, while those only moderately disturbed need 7½ grains at times. Experimentation with clinical evaluation of each injection is required. Patients with depression usually have a better response to the smaller doses. Most patients with psychosomatic disorders seen in internal medicine require only 3¾ grains for therapy.

Adjunctive psychotherapy in the form of suggestion, persuasion, reassurance, explanation, interpretation, counseling, re-education, and guidance is carried on during the initial period of light narcosis. When the patient is in a hypnotic state, he is told that he will be cured; he is given a short and pointed explanation as to the cause and origin of his symptoms; he is spoken to in suggestive and reassuring tones. However, the patient's enhanced receptivity and amenability to suggestion and guidance persist even after he awakens; so psychotherapy can also be effectively employed postinjection with the patient fully awake and sitting up. The recommended procedure is to limit psychotherapy during the injection to the first three or four injections, and with subsequent injections, psychotherapy is employed after awakening.

With the use of intravenous amobarbital sodium and with increased experience by the therapist, most cases of psychosomatic disturbances in internal medicine can be adequately handled with only 15 to 30 minutes of added counseling and guidance. But adjunctive psychotherapy, while always desirable, is not essential for successful amobarbital sodium therapy. Many patients, especially those without situational stress, do not need involved psychotherapy and are relieved with just the drug and some suggestion and reassurance.

In cases in which emotional disturbance is associated with organic illness, it is imperative that the organic illness be concomitantly treated in the conventional manner, e.g., diet and antacids for peptic ulcer, antirheumatics for arthritis. In these situations, where emotional tension is associated with organic illness, the internist, by conjointly treating the disturbed psyche and the deranged soma, will be practicing "total" medicine.

ORAL VERSUS INTRAVENOUS USE

Amobarbital sodium given orally or intramuscularly has an entirely different effect from the intravenous form. Oral usage does not produce the hypnotic effect necessary for diagnosis or analysis, nor the narcosis requisite in therapy.

As compared with the frequent occurrence of hangover and headache after oral

administration, intravenous amobarbital sodium is rarely followed by these side effects, and almost never induces excitation, irritability, depression, or mental dullness

This vast difference in physiological effect is probably due to the sudden flooding of the cerebral centers when the drug is given intravenously, as contrasted with slow cerebral contact with oral use. However, other factors may operate to produce this difference in action, e.g., chemical conversion or modification of oral barbiturate by the stomach or liver before the drug enters the cerebral circulation.

ADVANTAGES OF AMOBARBITAL OVER THIOPENTAL

Amobarbital sodium is a hypnotic; thiopental sodium is an anesthetic. The hypnotic dose for thiopental is very close to the anesthetic dose. If anesthesia is produced with thiopental, the therapist is faced with the burden of the care and possible respiratory complications of an anesthetized patient. This necessitates the constant presence of oxygen, means for maintaining an adequate airway, stimulants, etc. Amobarbital sodium in the dosage used in this study, never produces anesthesia.

Thiopental is a dangerous drug. In the occasional thiopental-sensitive patient, even as little as $^3/_4$ grain can produce cessation of respiration and circulatory collapse; this never occurs with amobarbital sodium. Also, thiopental deaths are not unknown.

Amobarbital sodium is of much greater value in diagnosis and analysis. The dose for relaxation is much lower than that for hypnosis. The dose of thiopental for relaxation is the same as that for hypnosis or clouding of consciousness. Therefore, amobarbital produces much more useful emotional and verbal expression and ventilation, while thiopental can fail in this respect.

Violent verbal and motor abreaction almost never occurs with amobarbital sodium, while with thiopental it is of frequent occurrence. The author considers intense abreaction both unnecessary and undesirable in the great majority of psychosomatic disorders seen in general medicine. Further, violent abreaction is unmanageable in office practice. An exception is where the therapist desires the abreactive reliving of a recent and severe traumatic experience (war), in which case thiopental would be preferred.

In the author's experience amobarbital sodium is far more effective therapeutically than thiopental. This marked difference in action between thiopental and amobarbital is not generally recognized and has never been precisely delineated. And since thiopental was so widely used in World War II, most physicians have come to associate narcoanalysis and narcotherapy with this drug, with resultant disservice to amobarbital narcoanalysis and therapy. The author has met not a few psychiatrists who used thiopental in the Armed Services during World War II, but who were reluctant to use it later in civilian practice because of its depressant effect on respiration and the not infrequent occurrence of dangerously deep narcosis and violent abreaction, which are unmanageable in office practice. And holding the erroneous opinion that thiopental and amobarbital are similar in action, they also abandoned the latter.

Other factors have been the widespread belief that repeated injections of amobarbital sodium can be toxic and addictive; the belief that large doses of the drug must be used, with subsequent long recovery periods; and the failure to recognize that intravenous amobarbital sodium, apart from its analytical and diagnostic value, is also therapeutic in itself.

LIMITATIONS AND EXCLUSIONS

Amobarbital sodium has value in diagnosis and in relief of the anxiety and depressive components, but usually does not change the basic abnormal patterns of marked character disorganization, e.g., psychopathic personality, fixed personality disturbances, inverse sexuality, ingrained character defects, character neurosis, and rigid neurotic patterns. It is of greater use and benefit, but has variable therapeutic results, in severe and fixed emotional disorganization; deep-seated anxieties, with or without somatization, of years' duration; and obsessive-compulsive states.

Amobarbital sodium should not be used therapeutically in schizophrenia; manic states; psychotic depression; involutional melancholia; paranoia of any fixed or prominent degree, or of a primary nature; organic psychoses and dementias.

SAFETY OF METHOD

In 1532 patients who received 12,154 injections in the author's office from 1944 to 1954, under the conditions of slow administration and maximum doses of 7½ grains, there were no instances of adverse reactions or toxic effects.

In the first two years, periodic Bromsulphalein liver function tests, urinalyses, nonprotein nitrogen tests, and blood counts were done on patients who were receiving injections for more than two months. Indications of liver or kidney damage were never found. Three patients received injections periodically for one year with no evidence of toxicity, habituation, or addiction.

There are no absolute contraindications, as the drug was safely given to patients with severe hypertension, acute bronchial asthma, acute coronary thrombosis, cardiac decompensation, and arteriosclerotic senility. However, with these conditions, caution, in the form of smaller doses and slow administration, should be exercised —especially whenever liver or kidney function is impaired.

HABITUATION, ADDICTION, TOLERANCE

The early fears of habituation or addiction were never realized: Not one case of habituation or addiction was observed. For a drug that is capable of producing instantaneous relaxation and calmness in tense and anxiety-laden patients, this is a remarkable characteristic. Patients were treated for as long as four to six months without habituation or addiction. When told they have had sufficient treatment, they neither object to the discontinuance nor ask for more injections. This is in marked contrast to oral use of barbiturates, where habituation is always a possibility. Actually, oral habituation disappears with intravenous therapy.

Tolerance does not develop; instead, smaller doses suffice with increasing injections. Accumulative effects are not seen.

CONCLUSIONS

1. Narcoanalysis and narcotherapy with amobarbital sodium is of undisputed value in psychosomatic management, but is rarely used in internal medicine. It is ideally suited for the internist, and can be easily used by him with great advantage to aid and facilitate the psychosomatic diagnosis and therapy of his practice.

2. To those without previous knowledge or skill in analytical or hypnotic technique, the continued use of amobarbital analysis and therapy will enlarge understanding and insight into the psychic disorders, and will acquaint the internists with a rapid and easily used technique of psychosomatic evaluation and therapy of the emotionally disturbed patient.

3. Further, use of narcoanalysis and narcotherapy by physicians in internal medicine would help arrest incipient emotional illness before rutted patterns are established; would decrease the growing organic illness initiated by emotional distress; and, through obtainment of gratifying results, would stimulate the internist to the use of additional psychosomatic techniques, and would inspire him toward original and higher goals of psychosomatic diagnosis and therapy.

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U. S. Population Figures Released

Figures released by the Census Bureau indicate that the population of the United States was approximately 172,790,000 as of Dec. 31, 1957. The estimate represents a 3 million increase over the preceding year, and a 22 million gain since 1950. The bureau reports that births and deaths in this country both reached a record high during 1957.

Promazine in the Treatment of the Discharged, Agitated, Senile Patient

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The ultimate objective in the use of the phrenotropic compounds in treating patients institutionalized for senile agitation is their eventual restoration to the home environment. If the hypermotricity and anxieties remain safely controlled with the patient returned to the milieu in which these disturbances initially flowered, one could envision a fuller, more normal life for these disturbed aged persons.

As indicated in a previous paper,* the true testing ground of adequate sustained tranquilization is the home; here many of the patient's conflicts and hostilities first were nurtured and developed; long-standing antagonisms and aggressions could readily be re-created by contact with the original victim or instigator of these feelings. The ability to weather this trauma would appear to be the basic criterion for effectiveness of the ataractic compound.

This study describes 22 discharged senile patients whose agitation was successfully controlled in a modern nursing home under continuous promazine† administration and who were discharged on a minimum maintenance dosage for home care.

METHOD

The only requirement for including a patient in this study was adequate control of his agitation by promazine while he was a patient in the nursing home. Twenty-two consecutive dischargees, ranging in age from 60 to 85 years, were requested to continue taking the minimum effective dosage of promazine without interruption after returning home. There were 15 women and 7 men.

Their pattern of activity before taking promazine had been sufficiently disturbed to preclude their remaining at home. When all previous measures to control hypermotricity had failed, their physicians had them admitted. Generally, their conduct was characterized by rage, hyperexcitability, restlessness, temper tantrums, aggressiveness, assaultiveness, prevarication, disorientation, poor personal hygiene, and destructiveness. A combination of three or more of these factors warranted classification as severe agitation. Diagnostically, they fell into four psychological groupings: Simple senile agitation, 13 patients; anxiety neurosis with agitation, 5; agitation with carcinoma, 2; senile psychosis, 2. Their physical ailments were distributed as follows: Arteriosclerotic cardiovascular disease, 6 patients; cerebral arteriosclerosis, 4; gastrointestinal disturbances, 4 (2 cholecystitis, 1 ulcer, 1 colitis); bronchiectasis, 3; carcinoma (rectal, pulmonary), 2; pulmonary cyst, 1; Parkinson's disease, 1; malignant hypertension, 1.

When ready for discharge from the nursing facility, the patients' responses had

* Settel, E.: GP *14*:97, Nov., 1956.

† The trade name of Wyeth Laboratories for promazine is Sparine.

been classified as excellent in 13 cases and good in the remaining 9. After 12 to 22 weeks of therapy their symptoms at the custodial institution had abated sufficiently for them to enjoy improved interpersonal relations with nursing personnel, physicians, other patients, and visiting members of their families. In addition, anxieties about their physical ailments had also diminished to a point where their symptomatology was readily controlled. At this stage, both the responsible members of their families as well as the administrators of the nursing home felt that these patients were ready for the more precarious environment of their homes.

A personality profile study was drawn up on each patient as a control against later behavior patterns (see table I). A reliable member of each family who was in close contact with the patient was designated as the official observer to report on specifically designated items on the profile.

Weekly visits were made to the home by the writer or a psychological social worker. Interviews and/or physical examinations were conducted at these visits to determine any changes, either positive or negative, in both behavior and physical condition. Laboratory tests (including urinalyses, hemograms, renal and hepatic

TABLE I

Personality Profile Chart

Eating habits	Appetite: Diet: Good ( ) Fair ( ) Poor ( ) Overeats ( ) Varied ( ) Monotonous ( ) Eating behavior: Good ( ) Adequate ( ) Poor ( ) Tremor when eating? Yes ( ) No ( )	Comment:
Sleep habits	Average hours of sleep per night hrs. Restless ( ) Up during sleeping hours ( ) Sleeps with light on ( ) light off ( ) Sleeps guarded ( ) unguarded ( ) Incontinence: Urine ( ) during night ( ) during day ( ) frequently ( ) rarely ( ) Stool ( ) during night ( ) during day ( ) frequently ( ) rarely ( )	Comment:
Personal hygiene	Keeps self clean: yes ( ) no ( ) washes self ( ) needs help to wash ( ) Keeps clothes clean and neat: yes ( ) no ( ) dresses self: yes ( ) no ( ) Attention to personal hygiene: above average ( ) average ( ) below average ( )	Comment:
Emotional traits	(check where appropriate) Hostile ( ) Angry ( ) Assaultive ( ) Loving ( ) Destructive ( ) Restless ( ) Aggressive ( ) Friendly ( ) Dishonest ( ) Envious ( ) "Bossy" ( ) Manageable ( ) Poor judgment ( ) Other ( )	Comment:
Occupations	Has a job ( ) part time ( ) full time ( ) Works around the house ( ) Does nothing ( ) Other:	Comment:
Recreations	Reads—frequently ( ) occasionally ( ) never ( ) Listens to TV, radio—frequently ( ) occasionally ( ) never ( ) Other: (games, etc.)	Comment:
Interpersonal relationships	Excellent Good Fair Poor With Family ( ) ( ) ( ) ( ) Friends ( ) ( ) ( ) ( ) Physician ( ) ( ) ( ) ( ) Clergy ( ) ( ) ( ) ( )	Comment:
Additional comments:		

TABLE II

Results at Home in 22 Cases

Result	No. patients	Per cent
Excellent	11	50
Good	8	36
Poor	3	14

function tests) were performed at five to six week intervals to preclude or anticipate any possible side effects.

The period of clinical observation was continued for four to five months in all 22 patients observed.

The average dosage of promazine administered in this series was 25 mg. three times a day. In the event there was any complaint of insomnia, a bedtime dose of 50 mg. was added. In the case of the 2 patients with senile psychosis, the maintenance dosage was 50 mg. three times daily in 1 and 100 mg. three times daily in the other.

RESULTS

Of the 13 patients who had demonstrated excellent response while at the nursing home, 11 (85 per cent) continued to behave in exemplary fashion at home. A high level of interpersonal relations persisted with members of the family, friends, neighbors, and clergy. Many of the patients were assigned minor chores to perform around the house and were able to assume these small responsibilities without difficulty. Among some of the duties that these 11 performed were light cleaning and dusting, gardening, and shopping.

The remaining 2 patients from the group classified as excellent at the nursing home were not quite as restrained at home but exhibited sufficient restraint to fall into the good group. In these 2, the reawakening of hostilities against close members of the family (spouse in 1 case, daughter in another) became a traumatic experience. The 2 patients became cross and irascible occasionally but seemed able to resume a tranquil level of behavior after one or two explosive outbursts.

Eight patients of the total of 22 (36 per cent) responded on a good level. Two of these, as mentioned, were from the original excellent group, while 6 of the 8 sustained the same good effect they had demonstrated before.

Only 3 patients of the 22 (14 per cent) reverted back to an agitated state, and in each of the 3, the etiology of the emotional relapse could be traced to a provocative factor present in the home environment but absent at the nursing home. In all 3 instances the patients were left alone at home all day while members of the family were at work. There was a measurable degree of panic and fear at being suddenly left alone after being carefully watched in the relative security of the nursing facility. This basic insecurity was converted into anger, rage, restlessness, and agitation. One of the families took cognizance of the state of affairs and resolved the situation by having a married daughter remain at home with her disturbed mother. The

remaining 2 patients were obliged to return to the protective milieu of the nursing home, where serenity promptly returned.

The 2 senile psychotic patients were able to remain at home with a good behavior level, although their usefulness in the house was of a very limited nature.

SIDE EFFECTS

The only side effects noted during the course of administration of promazine were two transient episodes of vertigo, which subsided after discontinuance of medication. On resumption of therapy after a three day rest period, the dizziness did not return.

There were no episodes of dermatitis, allergies, or gastrointestinal or cardiorespiratory side effects. Somnolence did not occur in any of the patients on promazine.

Repeated blood counts, chemistries, and urinalyses did not reveal a single instance of toxicity. It is well to note that all these patients had been on promazine therapy for long periods before discharge to the home and did not react unfavorably at the nursing home either.

CASE REPORT

L.C., a 74 year old woman with a long-standing history of arteriosclerotic cardiovascular disease, diabetes mellitus, and coronary insufficiency, had suffered progressive deterioration of her personality after the death of her husband. She became impatient and overdemanding of her married children, criticized them often and without due cause, went into temper tantrums and uncontrollable episodes of shouting and crying. She intentionally departed from the restrictions of her diabetic diet and frequently neglected to take insulin. She had recurrent mild acidosis.

At this point, her desperate family had her admitted to the nursing home. Here the diabetic imbalance was rapidly controlled by exercise of vigilant supervision of diet and insulin requirements. However, despite the more sheltered atmosphere of the nursing home, her agitation became progressively worse.

She was put on 50 mg. of promazine three times daily and within five days became quiet, less abusive and aggressive, and began to enjoy relatively good social relations with other patients and staff. After nine weeks at the nursing home, she was discharged on a maintenance dosage of promazine (25 mg. three times daily).

At home, members of her family were extremely amazed and gratified at the return to normalcy of her temperament. She again became affectionate and interested in the affairs of her family. Her physical complaints subsided to a minimum; she kept within the limitations of her diet and took insulin regularly. She began to do some cooking and baking for the family and tried hard to please them. There were no toxic effects after seven continuous months of therapy with promazine.

DISCUSSION AND CONCLUSIONS

The implications of this study are manifold. The over-all problem of a rapidly increasing geriatric population carries with it the concomitant increase, both relative and absolute, in the incidence of senile agitation. Our already overburdened public and private facilities for adequate care of these disturbed persons are at present a matter of considerable concern on the highest government levels. In addition, the shortage of adequately trained personnel to staff every type of hospital and nursing home facility remains a serious hindrance to any sizable expansion program.

The development of a safe and effective ataractic compound may provide a large part of the solution to these problems. The eventual restoration of these agitated

aged patients to the home environment represents a desirable end point from both the medical and sociological viewpoints. The latter years may become, for these people, a golden era of peace and usefulness rather than one of burdensome desperation for their physicians and families.

Promazine represents a safe and effective normalizing agent in senile agitation Of 22 discharged nursing home patients who had been adequately controlled in the restricted and sheltered confines of institutional life, only 2 could not cope with family settings and had to be returned. Even in these failures, it is believed that readmission might have been avoided had some member of the family been able to remain at home with the patient during the daytime hours.

The remaining 20 patients continued to function on a good to excellent level and found a limited area of usefulness in the family life.

There were no side effects of any consequence. At this writing the patients are happily engaged in making a fuller and more purposeful life for themselves in their later years.

ACKNOWLEDGMENT

The promazine used in this study was supplied by Wyeth Laboratories, Philadelphia.

SYMPOSIUM ON MEDICINE AND WRITING

The Symposium on Medicine and Writing that appeared in the November 1956 issue of INTERNATIONAL RECORD OF MEDICINE has been published recently as a Monograph. The articles included in this Monograph are: "The Editing of a Modern Medical Textbook" by Russell L. Cecil; "Plain Talk and Clear Writing" by Morris Fishbein; "The Principles of Bibliographic Citation" by John F. Fulton; "The Art of Communication" by Joseph Garland; "On Writing a History of Medicine" by Douglas Guthrie; and "Minerva and Aesculapius: The Physician as Writer" by Félix Martí-Ibáñez.

This 72-page Monograph is sold for $3.00. As the fourth in the series of MD International Symposia, this book is the companion piece of *Medical Writing*, which was published in May 1956.

To obtain this monograph, write to MD Publications, Inc., 30 East 60th Street, New York 22, N. Y.

RUPTURED ARTERIES IN FRACTURES. A radioactive tracer method being developed to determine whether fractures of the femur's neck have ruptured arteries nourishing the head of the femur was described by Dr. Hugh Smith at the Alumni Postgraduate Convention of the College of Medical Evangelists, Los Angeles. This severing of the blood supply is said to be a major cause of the fracture's failing to knit. P^{32} is injected into the blood. During the surgery to repair the fracture, a small geiger counter is inserted into the head of the femur through the medullary canal. If the count is high, or reasonably so, the circulation has not been cut off.

DRUG CONTROLS RADIATION SICKNESS. Twenty-five of 40 patients treated with a meclizine-pyridoxine tablet (Bonadoxin, Roerig) to prevent postirradiation nausea and vomiting experienced "dramatic and complete relief" or definite improvement (Lofstrom et al, West. J. Surg. 65:306-307, 1957). Only 2 in a control group of 15 patients treated with a placebo were relieved of symptoms, and no negative effects were noted from the meclizine-pyridoxine.

"NEW TYPE" OF ANGINA. Clinical and experimental observations on a "new type" of angina pectoris were reported by Dr. Myron Prinzmetal and associates to the Western Society for Clinical Research, Carmel, California. The angina occurs at rest; attacks are infrequent; pain is severe and prolonged. The angina is apparently due to almost complete occlusion of a relatively large single coronary vessel. An associated spasm causes interruption of blood to a large area of the myocardium. Use of anticoagulants in this "new type" of angina is absolutely indicated, Dr. Prinzmetal said.

CHLORPROMAZINE FOR TETANUS. Administration of chlorpromazine, in conjunction with barbiturates, in 7 cases of tetanus, 5 of them severe although not fulminating, was effective in controlling convulsions (Brit. M. J. 1:16, 1958). All patients recovered, and no serious untoward effects were observed from intravenous infusion of large amounts of chlorpromazine.

NONEXPLOSIVE ANESTHETIC INTRODUCED. A new and potent non-explosive anesthetic (Fluothane, Ayerst) has been introduced to aid surgery in the U. S. A fluorinated hydrocarbon first synthesized in England in 1951 as trifluorobromchlorethane, it is said to have many advantages over ether and chloroform, has been successfully used in 20,000 clinical trials in England, Canada, and the U. S. since 1956 for almost all known operative procedures in patients of all ages and conditions, and has exhibited essentially no adverse side effects.

DEATHS OF CHILDREN FROM ACCIDENTS. More children aged 1 through 14 years will die from accidents during 1958 than from all known childhood diseases, predicted Dr. H. A. Matthews at the 13th National Conference on Rural Health of the American Medical Association. More than 4000 children will die from automobile accidents, 2000 from drowning, 1500 from mechanical suffocation, 2000 from burns, 400 from poisoning, 700 from falls, and 500 from firearms, he said. Mentally and emotionally disturbed children often become accident casualties under ordinary safe conditions, while a healthy child becomes a casualty in direct proportion to the hazards of the environment.

OINTMENT SPEEDS WOUND HEALING. An ointment containing a combination of papain, urea, and water-soluble derivatives of chlorophyll was found to speed healing of infected surface wounds by surgeons at the Fort Howard, Md., Veterans Administration Hospital. The treatment produced excellent results in 100 of 106 infected wounds, good results in one, and poor in five. In the five cases of poor results, gangrene was present and the blood supply to the infected areas was extremely poor. However, good results were obtained in 4 patients in whom gangrene was present.

REFRIGERATED HEARTS OF DOGS RESUME NORMAL FUNCTION. Hearts of small dogs were refrigerated at 4 C. for six to eight hours and, when transplanted, returned to normal function, reported Drs. Watts R. Webb and Hector S. Howard to the Southern Section, American Federation for Clinical Research. Hearts were removed from small dogs and either perfused to remove all blood elements or injected with large doses of heparin amounting to 10 mg./Kg. body weight. After refrigeration, the hearts were transplanted into the necks of larger dogs where they maintained their usual cardiac output until the transplants died. The average length of life was about two days.

Medicine in the Spain of Don Quixote

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I. SPAIN IN SPACE: THE COUNTRY AND THE PEOPLE

The Spain of Don Quixote was the Spain of the late years of Philip II and the early years of Philip III, or the latter half of the sixteenth century and the first decade of the seventeenth. It was still the Spain of the Golden Age, but already turning to silver, and at that somewhat tarnished. It was in this period of Spanish history that Don Quixote rode across the fields of Montiel, leaving the imprint of his romantic whimsies on the face of Castile, at that time the face of the civilized world.

The Spain therefore portrayed by Cervantes was the Spain of the Golden Age, which covered two centuries of Spanish history and summed up the history of Renaissance Europe. For some time, Spain had yearned to shed its touch of Africa and become European. This yearning was translated into such an explosion of the will to conquer, that Spain ended by being truly universal. Once this cycle was completed, Spain, exhausted by the effort, regressed in the seventeenth and eighteenth centuries and has remained so to this day through its unhappy fate in our time.

In space, as seen on the map, Spain is like a massive head gripped by the hair by Europe. African by its geographical position—its position in space, European by its history—its projection in time, Asian by its anthropological origin, American by virtue of its conquests, Spain geographically is the most Occidental and spiritually the most Oriental of all the countries in the European continent, a continent so crowded that sometimes it must erupt in order to release the mighty forces constantly bubbling inside it.

Such an eruption was the conquest of the New World, the greatest, most heroic venture in Western history. In that undertaking, a handful of semiliterate men, impelled more by their dreams than by the winds that billowed the sails of their vessels, embarked upon the navigation of alien waters until then known only to the stars in the American skies.

In Spain the spirit of Africa is alive in the blazing—honey and wax—paintings of El Greco, while that of Europe throbs in the subtle wonders of Velázquez's pastorals. The spirit of Africa blazes also in the very personality of the Spaniard, an Arab at heart, with all of the latter's delight in startling colors and outlandish meals and his propensity to violent rages and wild passions.

On the other hand, Spain is a lamp shedding light over Europe with her art: Cervantes' influence is noticeable in the French and English literature of the seventeenth and eighteenth centuries; Calderón de la Barca's poetry gave inspiration to Shelley, and Goya's paintings to Whistler and to modern surrealism. In its great

epoch of American colonization, from 1516 to 1700, Spain was the spiritual creator of twenty nations and her influence was their mainspring, as Greece was of Egypt and Asia Minor in classical times.

Spain's geographical position has been both her might and her misfortune. The Pyrenees, the Atlantic, and the Mediterranean isolate her from the rest of the world. Bristling with mountains and riddled with rivers, she nevertheless suffered innumerable processions of invading races: the Iberians, a Hamitic-Semite race of North African origin, Cro-Magnon in type; Afro-Semitic races; Tuaregs; Copts; and Kabyles from the Sahara. Spain was in the beginning an African country peopled by Africans, from whom the Spaniards themselves are descended. These were followed by Celts, Phoenicians, Greeks, Carthaginians, Romans, Vandals, Visigoths and Swabians, Arabs, Berbers, Almohades, Almoravides, Jews, and, at long last, the Spaniards themselves when Spain became an independent nation upon the union of Aragon and Castile in 1479 with the marriage of Ferdinand and Isabella.

The geographical situation of Spain in the extreme west of the Mediterranean and the extreme south of the European continent has been, at least to a certain extent, a determinant factor in her historical destiny. Spain was the last refuge for people emigrating from the Orient by sea, for beyond Spain there was nothing but the *mare incognito*, the frightening *non plus ultra*. For emigrants from the North, Spain was the extremity of the continent, the last point at which they could replenish their strength before jumping into the fearsome mysteries of the African mainland.

Since ancient times Spain, with that prodigious faculty to absorb intruders she has always had, accepted and absorbed Phoenicians, Greeks, Carthaginians, Romans, and Visigoths. In the dawn of the Middle Ages, with the Moslem invasion in the eighth century, the exclusiveness of the Mediterranean was broken and thereafter new routes and new ways of life were adopted.

For seven centuries Moslems and Christians lived side by side in Spain, and, what is more important, they lived for the most part in peace and harmony. From this union was born the social class of the Mozarabs, or Moslems, living in accordance with Christian laws. For seven centuries periods of intolerance alternated with periods of collaboration, which is not difficult to understand if we recall that in the thirteenth century the three religions, Christian, Mohammedan, and Jewish, held services in one and the same place of worship, the Mosque of Santa Maria la Blanca in Toledo.

II. THE GOLDEN AGE

It was toward the end of the fifteenth century, at the time when Cervantes was an adventurous youth, that Spain became a decisive factor in Western history. This burgeoning was determined by the destruction of the last Moorish outpost in Spain, which together with the conquest of America led to a remarkable rise in Spain's influence on the European continent.

Spain's Golden Age lasted almost two hundred years, but no two historians agree on the actual beginning or end of this period. As far as we are concerned, we may say it stretches at least from the birth of Charles V in 1500 until the Peace of West-

phalia in 1648. During that period the Spanish monarchy became a token of Spain's world hegemony, to which was added the idea of the spiritual universality of Roman Catholicism.

Spain's Golden Age, the setting for Cervantes' life and the exploits of Don Quixote, included the reigns of Charles V and the three Philips. Within this period there took place the unification of Castile, León, and Aragon; the conquest of Granada by Ferdinand and Isabella; the epic of Columbus and his ships; the victories of the Duke of Alba in Flanders; the conquests of Mexico and Peru by Cortes and Pizarro; and the battle of Lepanto in 1571 which halted the Turkish invasion. With El Greco, Velázquez, Lope de Vega, and Calderón, Spain reached the pinnacle of glory, just as its decline and fall began with the politics of Philip III.

During the Golden Age Spain continued the wondrous process of integration initiated at Toledo in the thirteenth century, when, in the greatest example of tolerance ever known in history, Christians from all parts of Europe met with Arabs, Jews, and Castilians at the College of Authors in Toledo. In that epoch of Byzantine Spain, Toledo could boast that all three religions, the Jewish, the Mohammedan, and the Christian, officiated in the same place of worship and dispensed to their respective faithful what each believed to be the True Word. This integration process ended toward the end of the fifteenth century with the expulsion of the Jews and the Moors and the persecution of heretics.[A]

In the fifteenth century the King of Spain was still the principal arbiter on earth. A Spaniard could go practically anywhere throughout the civilized world without treading alien ground. In Europe one language, Latin, and one faith, the Catholic, were supreme. This period of Spanish predominance was, however, more the reward of chance and the fruit of inheritance than of legitimate effort. In contrast to the great armies and the powerful circles of the Court, the common people were in great poverty. Inflation was on the increase. The Golden Age was in fact an age of copper, the coin of base metal being by far more abundant than the gold doubloon.

But the Spanish nation was living in the full bewitchment of a legend. A fabulous navigator was conquering a new world; the galleons kept returning laden with treasure, spices, and befeathered Indians resplendent as birds of paradise; ragged but invincible hordes of Spaniards were overrunning Europe; a chairbound monarch overcame the legendary Ottoman at Lepanto on the silver and blue waters of the *mare nostrum*, and erected in the Escorial marvels wrought in stone.

This atmosphere of enchantment finally destroyed the spirit of Don Quixote. For from the bowels of the bold vessels plying the American waters were born the fops, drones, and rogues who later plagued the Spain of Don Quixote.

The atmosphere was a mixture of excessive national pride, laziness, collapse of the spirit of idealism, bigotry and fanaticism, sexual license, cruelty, frivolity, arrogance, and, to a certain extent, indifference to universal principles.

More than half the population of Spain consisted of nobles; the rest were beggars and vagabonds. Fanaticism ran cheek by jowl with sorcery. The wanton flirtation of the nobles often ended in bloody brawls that embroidered in red the silks and satins of their ladyloves.

Brigands, cutpurses, and students made it impossible for respectable people to

venture abroad at night without an armed escort and blazing torches. Religion, sadism, and licentiousness frequently formed an unholy trinity, as in the mysteries of the sect of *Alumbrados* at the convent of St. Placidus. Lovers presented their sweethearts with souvenirs of linen soaked in the blood shed in their brawls. And Don Juan, kissing his inamoratas between wrangles and corpses, covered his victims' tombs with roses of passion.

III. THE SPAIN OF DON QUIXOTE

The Spain of Don Quixote was a Renaissance stage but with Gothic cathedrals all over. It was a period of wandering, when even the Royal Court moved from place to place as if it were a mere encampment of soldiery.

The rich, sonorous Castilian tongue already vibrated in the clear renaissance prose of Castile. Garcilaso's poems found their way into the pockets of Spanish soldiers throughout the empire and were sung to the strum of guitars. Mystic imperialism was now opposed to the humanistic and humanitarian tradition of the Middle Ages. The realist tradition was imposing itself in great strides. And one day the filigree verse of Góngora, the ornate architecture of Churriguera, and asceticism would take the place of Cervantes.

Two worlds were already fighting each other in the Spanish conscience. Calderón would maintain that life was a dream; Góngora would affirm that nightingales were nothing but "music of the mind." Cervantes himself before them would say, through the lips of Sancho Panza, that windmills were not giants; and Don Quixote would finally end by calling an inn an "inn," after having called it a "castle" to compensate for those prosaic souls who would make even a castle into an inn.

The picture of the Spain of Don Quixote, the Spain of the beginning of the seventeenth century, was sad and somber. Despite the galleons from America, creaking under the weight of the gold they carried, poverty and hunger reigned throughout the Iberian peninsula. The lack of food and refreshment at the places where Don Quixote stopped, where there was nothing to eat "except what the traveler himself carried," the proverbial meagerness of the saddlebags of the ever-hungry Sancho, are tokens of the misery of the period. Even the nobles, living apparently in luxury and ostentation, like the dukes portrayed in *Don Quixote*, were actually riddled with debts and constantly confronted with starvation. Castile at the end of the sixteenth century was impoverished, and the needs of the clergy and the nobility exhausted all the gold arriving from the Indies. The nobles dissembled their misery with traditional Spanish pride, maintaining ever a haughty face to the greatest misfortunes, covering their famished bodies with threadbare cloaks and darned habiliments, fasting through sheer will power, like the *hidalgo* described in Mendoza's *Lazarillo de Tormes*.

But if the Spanish belly was empty, the Spanish mind was filled with dreams. Foreign ambassadors commented in letters to their sovereigns on Spanish splendor and extravagance. Don Quixote himself neglected the management of his estate and sold many acres of glebeland to buy books on chivalry. As soon as the bugle blew, the hungry nation jumped to arms, forgetting their troubles in their eagerness to

embark upon another great adventure. Meantime, the monarchs ground the nation down with new imposts and neglected the only flourishing industry that remained, vine growing, on which in 1604 the Duke of Lerma imposed outrageous taxes not without considerable protest from the people, which event perhaps is symbolized allegorically in Don Quixote's battle with the wine skins.

At other times, as under Philip III, the King's agents took possession of the gold and silver at the moment of unloading from the galleons for delivery to private individuals, leaving in exchange receipts not worth the paper they were written on despite the solemn promises to pay inscribed therein.[B]

The general abandonment of agriculture and all the useful arts and trades contrasted with the pinnacle reached in the fine arts. Youth was devoted solely to the exercise of arms and to seeking its fortune in the New World. Others sought shelter within the easy existence of the Church, and the ecclesiastical concourse increased so, that Brother Luis de Miranda delivered Philip III a memorial suggesting ways of impeding the waxing growth of the clergy. The same was done in Toledo by the lawyer Geronimo Ceballos and other illustrious men. Don Quixote alludes to the enormous number of friars, monks, and priests in chapter 8, part 2:

"Ah," replied Sancho, "but I have heard that there are more monks in heaven than knights errant."

"That is so," answered Don Quixote, "for the number of clerics is greater than the number of knights."

With the expulsion of the Moors, Spain lost the hands most useful in agriculture and the only ones successful in trade and industry. The number of Moors expelled was one hundred and fifty thousand, according to some authorities, and one million five hundred thousand, according to others.

The depopulation of Spain took on alarming proportions in the times of Philip III and Philip IV. The city of Burgos, which had more than seven thousand inhabitants during the time of Philip II, had barely nine hundred in the year 1624. León went from five thousand to five hundred. In Toledo more than a third of the residents were gone. Spain, in fact, became semideserted, so much so that the resultant lack of soldiery was the greatest obstacle in the carrying on of warfare.

The administration of justice was corrupted in the highest degree. The admirable laws that Spain had always possessed now no longer held valid even for the judges themselves. No one was safe even in the most important places. Cervantes' description of the notorious brigand Roque Guinart, who foraged under the very noses of the armed forces in Barcelona and mingled with highly placed personages in the city itself, confirms the gravity of the prevailing situation. In 1602, the very date when Don Quixote and Sancho came up against Guinart and his band of brigands, the Viceroy of Catalonia declared that the government was powerless to suppress banditry.

The Duke of Lerma[C] was blamed to a great degree for the disasters suffered by the nation during the reign of Philip III, just as the Duke of Olivares was blamed for those during the reign of Philip IV.

So bad was the situation that in 1590 Cervantes begged in vain for a government post in Guatemala. Had he been granted it, Cervantes might have ended up as just

another government bureaucrat buried in some obscure American mission, and Don Quixote would have never deployed through the landscape of La Mancha.

IV. GRANDEES, KNIGHTS, HIDALGOS, BURGUESES, AND LETRADOS

The structure of Spanish society was based on an intricate system of hierarchies. The *grandees* of Spain (dukes, marquesses, and counts) were the highest rank, being appointed by the king from among the most ancient lineages of the aristocracy. From a mere twenty-five grandees at the end of the sixteenth century, the figure increased to more than a hundred, all endowed with coronets on their shields and the right to remain covered in the presence of the king, to be called "cousin" by the monarch, and to make the queen stand up when they entered her quarters. The grandees of Spain were in the beginning valiant leaders in battle and later patrons of the arts and sciences, but in the end degenerated into a gang of favorites and flatterers.

After them in rank came the *knights*, members of the orders of chivalry of Alcantara, Calatrava, Montesa, and Santiago, who were conferred their right to arms by the king in the ritual of the accolade. One of these knights of the Order of Santiago was Calderón de la Barca, the immortal author of *La vida es sueño*.

The lowest class of the nobility were the *hidalgos* (the word *hidalgo* derived from the Spanish term "*hijo de algo*," somebody's son, or a "somebody"), scions of men raised to the nobility for their doughty service and merits during the *Reconquista*, the overthrow of the Moors. One of these hidalgos, living "in a certain place in La Mancha," was Don Alonso Quijano, later known as Don Quixote.

During the Reconquest a class of *burgueses*, or middle class, commenced to arise, whose privileges were later suppressed by the kings of the House of Austria. In contrast, the immigrants to Spain from all over Europe benefited more than these middle classes from the rich booty arriving from the New World. In turn, the indivisibility of the great estates owned by the Crown, the aristocracy, and the clergy, and the rights granted to these classes, particularly that of pasturage, which authorized their cattle to graze on the fields along their route, made the existence of a well-to-do agrarian class impossible. This lack of a middle class and husbandmen was one of the causes of the economic decline of Spain's Golden Age.

Finally, the *letrados*, that is, the nobles and burgueses devoted to humanistic studies through love of literature or as an apprenticeship to obtaining administrative positions at Court, increased in number as university instruction increased.

At the beginning of the seventeenth century, there were in Spain some thirty-two universities in existence, the oldest being that of Salamanca (founded in the year 1243), "a forum of all the sciences and virtues," at which in 1566 more than sixty professors were teaching and seventy-eight hundred students were registered. It was a bulwark for freedom of education; not only were women allowed to study there, but also to teach and even to bear the title of *docente*, it being also one of the few centers in the world where the dissection of corpses for the teaching of anatomy was permitted.

In the University of Alcalá de Henares,[D, E] next to Salamanca in prestige and

standing, according to Cervantes in his *Coloquio de los Perros* (*Colloquy of the Dogs*), two thousand of the five thousand registered students were studying medicine, which, commented Cervantes, was "a bad omen, since either everyone of these two thousand students finds patients to heal, which implies a great misfortune for the country, or they all die of hunger."

V. EMPIRE AND INQUISITION: THE "BLACK LEGEND" IN SPANISH HISTORY

In order to understand Spanish medicine in the Golden Age, that is, in the times of Don Quixote, it is necessary first to consider some of the problems—brilliantly discussed by Marañón—which, like dark clouds, have obscured from times of old the firmament of history and prevented our obtaining a clear, unfettered view of this epoch.

For many, too many, years the so-called "Black Legend" of the Inquisition has hung like a cloak of infamy on the shoulders of the Spain of the Golden Age. This black story was woven out of two basic ingredients: the Spanish imperialism of the period, looked upon as a military juggernaut which, with the aims of oppression and profit, bound the whole world in an iron belt; and the influence and power of the Inquisition, looked upon as the age-old enemy of spiritual and scientific progress.

That fable has been scattered to the wind as historical research has shown that the Spaniards were neither more nor less demanding than any other European empire; that they fostered to a remarkable degree the advance of literature and the sciences; and that, after the begored days of the Conquest, they granted the natives of what we nowadays call Latin America a social rank and human respect never granted before by any other colonizing power in history.

Moreover, the Inquisition, a mere political instrument which paradoxically had a "unifying" mission, in view of the decision of the kings of the period to unite an until then disunited Spain, was not really an obstacle to scientific progress. Many works today prohibited in Spain received the fiat and approbation of the Inquisition, which seldom blocked the way to any scientific contribution of real merit.[F]

VI. LACK OF PEACE AND PROSPERITY AND THE BACKWARDNESS OF SCIENCE

Science in the Spain of the Golden Age never achieved the same progress as the arts. For art can cohabit with poverty, but science, particularly pure science, needs the wherewithal to clothe and feed itself. In poor countries or in periods of want and penury, poets, writers, philosophers, mystics, painters, musicians, and saints have flourished and blossomed, their inspiration, clothed in the florid tunic of words and idiom, needing nothing more to fly than the wings of their own genius. On the other hand, the researcher and the scientist, though occasionally they have succeeded in penurious surroundings, as a rule require the support of their country and their time in order to be able to do their work.[G]

This is why in fifteenth century Spain, whose power and wealth contrasted with the dire poverty of the common people, so that the country was so to speak a mart

of mendicants loitering on benches of gold, only those physicians in the service of the rulers, as we shall see in due course, made important discoveries or clinical advances of real merit.

Art in Spain was at that time of more interest than science, perhaps from reasons of race and temperament. In the Spaniard, imagination always prevailed over logic and intuition over perseverance. Tenacity was a quality he lacked while impatience he had in abundance. All of which made scientific progress difficult.

To that must be added the notorious individualism of the Spaniard, which makes of every Spaniard a pinch of salt and pepper, which alone is enough to season his entire surroundings, but if more than one, like any excess of seasoning, can ruin everything. This is what happened in the actual compass of the Iberian peninsula.[11]

Spain knew only one hour in history when she worked as a team, and that was hundreds of years before the Golden Age, when King Alphonso the Wise gathered together Christian, Moslem, and Jewish scientific investigators and gave them the watchwords of simplicity and clarity, which is the pennon of true science in all ages and countries.

Although the Spanish monarchs of the Golden Age favored a discreet patronage of arts and sciences, they were in fact, as Marañón has pointed out, collectors rather than patrons. Philip II erected the Escorial as a temple, a museum, and a permanent exhibition of science and geography, but he did nothing to stimulate scientific research.

In Spain research had to be carried out at the cost of personal sacrifice. Science, however, cannot advance unless it is backed by peace and prosperity, which is the same thing as saying tranquility of mind and financial support. This is borne out by the fact that in periods of war, depression, great explorations, conquests, or colonization, entailing misery, penury, unrest, or a lack of mental peace or of general interest in anything but the great issue of the moment, scientific progress is practically paralyzed. On the other hand, it is frequently at such instances of great collective disturbance that progress in art is attained, for a state of agitation and unrest always stirs artistic genius.

In the Spain of the Golden Age the air was filled with the unrest characteristic of times when great new lands are being discovered, and minds were filled with a blind belief in the marvel of America and with pride in the greatness of their country, which in a single century had attained the foremost position in the world. All this fitted poorly with the spirit of modesty and intellectual sobriety so necessary for concentration on scientific tasks.

Only in universities and convents, the only two centers of learning in the Spain of the Golden Age, do we see the dawning of scientific conquests. Unfortunately, universities such as Alcala and Salamanca were dedicated more to theology and philosophy than to science, while the convents were brewing centers of political intrigue as well as of all sorts of news and rumors.

VII. ROYAL PROTECTION OF MEDICINE

The only thing that favored the advance of medicine was that only worthy doctors

were appointed personal physicians by the monarchs of the House of Austria. This meant that thereafter they could count on the financial assistance of the king and the benevolent eye of the Inquisition. Furthermore, since they had to accompany the monarchs in their warring expeditions, these physicians became men with a universal outlook, which explains the many-sided and humanistic direction of their work.

This same direction brought it about that even pedantic physicians, who at first sought to keep their science enwrapped in the mysterious cloak of the Latin language as a protection against the curiosity of the public at large, ended by accepting the clear language of Castile, which finally became the vehicle for the transmission of scientific knowledge throughout Spain.

It must be acknowledged, at all events, that the Spanish monarchs of the Golden Age contributed largely to molding that age according to their own idiosyncrasies. Charles V was extrovert Spain "stretching outward," devoted to war and the cultivation of humanism, which paradoxically enough are two ways to make an impression upon the rest of the world, that is, by force of arms and by force of mind.

Because of his incessant warmaking, Charles V had time for nothing else beyond selecting the Gobelins and pictures for his own palaces. But his royal decrees were sometimes favorable to the progress of medical thought. In his *Constitutio Criminalis Carolina* he laid down certain rules regarding physicians, creating the ranks of "Latin surgeons" for those who had completed full studies, and "five-year surgeons" for those who were excused from learning Latin. Ferdinand and Isabella had already authorized the practice of medicine and surgery in certain special cases by "practitioners," who obtained their diploma merely upon the payment of four gold escudos.

Philip II was Spain once more retired within itself and austere, a Spain that believed more in serried battlements and the mausoleum of the Escorial than in fine prows and flaunting banners; a Spain of strife in the universities, a Spain in which the soldier and the courtier predominated.

A protector of the arts and sciences, Philip II organized scientific expeditions to the Spanish possessions in America, founded an Academy of Mathematics in the Escorial as well as a magnificent library, and drafted a plan for the historical and geographic description of Spain by sending out numerous questionnaires.

In his proclamation of 1588 he extended the powers of royal physicians, requiring them to enter and leave the royal bedchambers or those of the royal children "always by the main door," to taste the wines at the royal table—as Dr. Recio de Tirteafuera did at the table of Don Quixote—and to use bezoar stone against skin eruptions. He also set down that the starting salary of a doctor should be sixty thousand maravedis and that great physicians like Valles should get an extra twenty thousand maravedis.

Under this ruler, Spain began to react against the obscurantism still rampant in Europe. The Cardinal of Seville himself condemned in a written work all superstition and sorcery. The "Divine" Valles dared to purge Philip II one day when there was an eclipse of the moon, remarking sarcastically: "Let's shut the window so that the moon won't know." Father Joseph Sigüenza in 1580 described Philip II's sickness at Badajoz (viral pneumonia), scoffing at the astrologer Juan de Meletio

because "until the last days of this year he failed to inform us of the colds and unnatural humors that would attack the inhabitants of the earth."

Philip III missed his opportunity for greatness by failing to exalt himself sufficiently to reach the heavens with the mystics or the ends of the earth with the explorers and colonizers. *Don Quixote*, written during his reign, was his only claim to glory—a reflected glory, at that.

Although Philip III showed little interest in the intellectual life of his country and in politics, which he left in the hands of his favorite the Duke of Lerma, during his reign the Escorial library increased notably, for in 1612 two Spanish sea captains captured several vessels belonging to the sultan of Morocco which were carrying more than three thousand Arabic manuscripts on poetic, philosophic, theologic, and medical themes, all of which were taken to the Escorial. A large portion of these manuscripts were destroyed by fire in 1671.

Spain's preoccupation with the health of her vassals is borne out by the statute signed by Philip III in 1560, stating: "Desirous that our lieges may enjoy long life and perfect health, we are taking the precaution of providing them with doctors and experts who shall direct and instruct them and cure their illnesses, and to this purpose Chairs of Medicine and Philosophy have been established in the more important universities of the Indies as shown by their articles of title. Furthermore, recognizing how much benefit will result to all our realms here and overseas from the discovery of and trade in certain plants, herbs, seeds and other medicinal substances which may lead to the healing and good health of human bodies, we have resolved to send at certain times one or more of our personal physicians to the provinces of the Indies and their adjacent islands."

In this last proclamation, Philip III fostered the study of therapeutics by counseling doctors to observe and report "all medicinal herbs, trees, plants and seeds there may be in their provinces . . . how they are cultivated, whether they grow in dry or damp places, and they shall write notes and indications of any trees and plants of different species . . . they shall conduct experiments and make tests of everything possible, of all medicines and herbs that there may be anywhere and that may seem remarkable to them, sending specimens to this Kingdom if they do not exist here." (*Digest of the Laws of the Kingdoms of the Indies*, Madrid, The Hispanic Council. Volume III, 1943, p. 139.)

In the same proclamation, another rule was aimed at quackery: ". . . the same rules and provisions shall apply in the Indies regarding those prohibited from acting as doctors, surgeons or apothecaries under the laws of Castile, and no one shall take the title of doctor, master or bachelor without having been examined or having graduated in an approved university."

Legal requirements for the practice of medicine and the duties of viceroys and governors in inspecting drug stores and medicines for the natives were also laid down.[1]

Philip IV, great patron and protector of the arts and literature and particularly of the theater, is worthy of sympathy. On the other hand, Charles III, with whom the glory of the Golden Age came to an end, deserves only pity for his many illnesses and for the hardening of the arteries which with him invaded the political body of Spain.

VIII. SPANISH MEDICINE AND MAGIC

Spanish medicine in the Golden Age inherited the magic of the fifteenth century, transforming it into an art in the seventeenth century, a century replete with superstition, witchcraft, astrology, and chiromancy, which bred the decay of Spanish scientific medicine.

Spain then was isolated from the rest of the world, more than by her formidable geographical barriers, the Pyrenees and the Mediterranean, by her arrogant imperialistic spirit, by the pride of being Spanish, which to the Spaniard was the same thing as being ruler of practically the whole of the known world. Scientific trends from abroad barely reached the country through those physicians who went to pursue their studies at Bologna or Padua.

Spanish medicine was mainly transmuter and transmitter. It tried to improve the healing methods inherited from the Moors when they were driven from Europe, and at the same time it Europeanized the ancient therapeutics, which had been Arabianized.

From America there was a considerable influx of knowledge of natural sciences. And from Italy, with Vesalius, there came in the middle of the sixteenth century an anti-Galenist impulse, which ultimately overcame the rigid influence of classic dogma. This great step forward toward modern physiology with the acceptance of Vesalius' teachings was made in Spain by Valverde (about whom we shall speak in more detail later) whose treatise, published four hundred years ago, in 1556, was more modern and morphologically advanced than Vesalius' own famous *de Humani Corporis Fabrica*. Valverde's revolt against scientific conservatism was supported by Vives, Pereira, Sánchez, and Servetus.

Once past the decisive decade from 1550 to 1560, Spanish medicoanthropological research, following the natural process of counterreformation, became more metaphysical and theological than physiological. The animal aspect—body and motion—of human "nature" was ignored; instead attention was concentrated on personal existence and personal moral freedom. Thus, while Harvey was creating modern physiology in England and Galileo physics at Pisa, Spain was developing the rights of man and the theological doctrine of medical science. While Harvey was arguing physiology with Riolan, Spanish Jesuits were arguing about *auxiliis* and human liberty.

From 1556 to 1648 (the Peace of Westphalia) physics and physiology in Spain were at no time of the same stature as her art, explorations, laws, and metaphysics. Against the expansionist European policy of Charles V, there arose like an insurmountable wall the defensive and "Escorialist" policy of Philip II, who "anchored the monarchy to the writing desk," and condemned Spanish medicine to empiricism and to renounce almost all scientific endeavor in favor of magic.

IX. THE DISEASES OF THE GOLDEN AGE

The diseases most frequent in Spain in the time of Cervantes were gout, exanthematous typhus, diphtheria, plague, intermittent fevers, and "buboes" or syphilis.[J. K]

Gout was so common as to give rise to the idea that Spain was the "cradle of the

disease," an idea borne out by the menus for the banquets of the period. On the occasion of his forthcoming marriage with the Marchioness of Alcaudete, the Count of Oropesa, in May, 1636, gave a great banquet consisting of "thirty appetizers, thirty desserts and ninety main courses." One of the meals planned by Martinez Montiño, the King's chef, included at one single sitting hams, capons, stewed mutton, pies, chickens stuffed with beans, trout, legs of mutton, custards, jellied veal pasties, small pies made of sweet dough, cold fowl in pastry blankets, ham stuffed with artichokes, fruits, pastries, cheese, preserves, jams, wafers, puddings, and junkets.

The treatment for gout was in fact very queer. Philip II's gout was treated even on Fridays, by virtue of a special papal dispensation, with meat, which because of the beef purines must have increased the monarch's uric acid. Philip II had, moreover, an allergy to fish, which gave him hives, especially in Lent, and later he suffered also from dropsy, ascites, and cirrhosis of the liver. The latter was probably syphilitic in origin and was somewhat checked by his rich meat diet.

This period was rife with badly treated syphilitic infections and purulent mouth lesions. There were also many fevers diagnosed as malarial, which were probably suppurative fevers caused by oral focal infections, as well as numerous cases of erysipelas. Disease and death occurred frequently and prematurely in the Spanish dynasties, probably because of consanguinity resulting from the practice of intermarriage for many centuries. Certain external characteristics, such as the Hapsburg underlip, a melancholy disposition, and renunciation of worldly pomps, were frequent in these dynasties. In contrast, the three children of Joan the Mad were extremely intelligent and well fitted for life.

Charles V was pale and taciturn from boyhood, had exaggerated cravings, suffered frequently from fever and heart attacks, became easily tired, and had dizzy spells and fainting fits. It has been impossible, however, to verify whether he was an epileptic. His Milanese doctor and companion devised the sovereign's motto, *Plus Ultra*. He had a huge outjutting lower jaw. Later he was tormented with gout, after which he contracted tertian fever, from which he eventually died.

Philip II, shortly after his marriage to his cousin Mary of Portugal, suffered from "pustulant dampness" of the skin. He also suffered from gout and tumorous swellings of the feet, leading later to acute dropsy and abscesses. Some people deemed him a schizophrenic because of his aloofness and constant withdrawals from the world. It is impossible to overlook the tragic picture, described by the Austrian ambassador, of this king when he summoned his children to show them, in the ambassador's words, "his malodorous body riddled with ulcers and infested with lice," that it might serve them as a warning on the transience of human glories.

Philip III was sickly and melancholic; Philip IV suffered from paralysis of the right side contracted three years before his death; and Charles II was a degenerate, with whom the famous dynasty that ruled in the Golden Age came to an end.

X. CHRONOLOGY OF THE GREAT

When considering the various aspects of medicine in the Spain of Don Quixote

we shall split the vast panorama thereof into various groups of physicians, more for the sake of clarity than of discrimination, since all these physicians after all shared the same love for the humanities and general knowledge. First we shall study the anatomists, then the surgeons, the nosologists, the epidemiologists, and those who worked on what we now dub medical specialties, specifically psychiatry, pediatrics, therapeutics, urology, ophthalmology, obstetrics and gynecology, and social welfare; and finally the humanists and the philosophers.

Let us consider first some famous events in Spanish history from the years 1545 to 1571. In that quarter of a century the following events took place, the mere reading of which sounds like the electrifying flourish of trumpets.

In 1545 El Greco was born. In 1547 Cervantes was born. In 1548 Andrés Laguna described the method of excision of vesicourethral caruncles. In 1549 Pedro Gimeno wrote his *Dialogus de Re Medica*. In 1550 Montaña de Monserrate published his "Anatomy." In 1551 the universities of Osma (Castile) and Lima (Peru) were founded, and Lobera of Avila published the first Spanish contribution to pediatrics. In 1552 Las Casas issued reports on the cruelty of the Spaniards toward the Indians. The year 1553 saw the foundation of the universities of Oropesa in Peru and Almagro in Spain, and also the University of Mexico; and in the same year Servetus gave a description of pulmonary circulation. In 1556 Valverde published his treatise on "Anatomy"; and in the same year Philip II commenced to reign. In 1557 Huarte de San Juan completed his *Examen de ingenios para las ciencias* (*Examination of Talents*), one of the earliest attempts to show the connection between psychology and physiology. In 1552 Lope de Vega was born. In 1565 the University of Baeza was founded, and in 1568 that of Orihuela. In 1569 Monardes published his *Materia medica* of the Indies. In 1570 Francis Bravo gave a description of spotted fever. And in 1571 Philip II attained victory at Lepanto.

XI. ANATOMISTS IN THE SPAIN OF DON QUIXOTE

The passion for anatomy. The roots of Spanish anatomy in the Golden Age are buried in the cultural subsoil of Italy, since it was in Italian universities that Spanish physicians studied.

At that time the mysteries of the human body were being opened to popular and scientific curiosity, just as overseas a vast and mysterious new portion of the planet was opening to the *conquistadores*.

The yearning to explore unknown lands ran parallel with that to explore the mysteries of the human body. Anatomy was taught on pure theory, but inquisitive physicians bolstered their scant theoretical grounding by keen observation of the wretched creatures who in interminable lines filed past them, mangled by the executioner or suffering from horrible diseases and plagues of such violence that in a few days they could turn a whole city into a charnel house.

Clinical teaching in Spain prior to the Golden Age was theoretical, and instruction in anatomy was reduced to a cursory study of the human body. Luckily, four years before Columbus' first journey, His Most Catholic Majesty King Ferdinand authorized (1488) the dissection of corpses at the hospital of Saragossa, whose motto was

Urbis et Orbe. The schools of Valladolid and Guadalupe followed. In Valladolid the first complete anatomy courses, of twenty months' duration, were given by Alonso Rodriguez de Guevara. These were published in book form in Coimbra in 1559. Gout-ridden though he was, like so many of his contemporaries, Professor Bernardino Montaña de Monserrate attended the classes in a litter, alleging that "anatomy is the alphabet with which anyone who wishes to be a physician must commence."

Modern anatomy, as is well known, was born in the sixteenth century from the work of Vesalius, who prior to being a physician at the Spanish Court from 1543 to 1564 crystallized in his *de Humani Corporis Fabrica* the point of view already foreshadowed during the decline of the *Quattrocento* by Berengario da Carpi and Leonardo da Vinci. Vesalius replaced the traditional dynamic descriptive method of the Galenists by a somewhat static but new method, which described the human body as a "workshop" or building, thus giving impetus to the development of "pure" anatomy.

Anatomists before Vesalius (Laguna, Lobera de Avila, Montaña de Monserrate). There was in Spain a group of writers, prior in time and ideas to the work of Vesalius, among whom the leading ones were: Andres Laguna (whom we shall study among the humanists), whose *Anatomica Methodus* pertains to the sphere of classic anatomy; Luis Lobera de Avila (whom we shall also consider later) whose *Libro de Anatomia* though of small importance in itself is the illustrative complement of the philosophical "dream" interpolated in his work; and Bernardino Montaña de Monserrate.

The latter owed his name to having been born, in the last decade of the fifteenth century, on the historic mountain Montserrat, a wild, steep sierra a few miles from Barcelona, where there still exists a ninth century Benedictine monastery with its famous *Moreneta*, the "Black Virgin," scene of the romantic legend of Parsifal and the Holy Grail, and where Ignatius of Loyola held vigil over his arms laid on the holy altar.

Montaña de Monserrate studied at Valladolid and possibly at Montpellier. He practiced in Valladolid and exercised an active mastery of his profession both in his professorial chair and in his book.

At the age of seventy, with forty-five years of professional practice behind him, he wrote his famous work, which already evinced, as against the architectural idea of anatomy current in the Renaissance, the first trends of the dynamic anatomy of the approaching Baroque period. His work was the second (Pedro Gimeno's in 1549 was the first) written by a pupil of Vesalius.

The title of Monserrate's work reads like a blurb in today's books: *Book of the Anatomy of Man, recently compiled by Doctor Bernardino Montaña de Monserrate, physician to His Majesty. A most useful and necessary work for physicians and surgeons desirous of perfecting themselves in their art, and available to other discreet persons interested in learning the secrets of Nature. Wherein is shown the structure and reparation of man, the way in which he is engendered and born, and the causes wherefrom he inevitably dies. Together with an interpretation of a dream occurring to his most illustrious worship Luis Hurtado de Mendoza de Mondejar, etc. which appears at the end of the present volume. Which dream, under a very elegant design, deals succinctly with the said structure of man, and everything else*

contained in this work. Addressed to my said Lord Marquess . . . Valladolid . . . Sebastian Martinez. In the year 1551

This lengthy, pompous title, beautifully printed together with the coat of arms of the Marquess on the cover of the book, epitomizes the solemn and theatrical spirit of the age. It indicates also the author's worthy endeavor to point out clearly the new path his anatomy was following.

Ten of the plates in this work were taken from Vesalius, and the text follows closely the pattern set by Henri de Mondeville's "Anatomy."

This was the first work on anatomy published in the Romance tongue (just as Valverde's was the first in the common tongue), so that anatomical vocabulary was enriched with terms taken from this tongue, which in turn acquired great importance together with scientific recognition.

The work contains, as an appendix or supplement, a curious and delightful story or "dream," in which the composition of the human body is represented by strange architectonic forms.

That "dream," as the one that appeared later in Valverde's work, held a double historical meaning, since it was both an expression of the urge to spread in medicine, which until then had been a closed science, and a genuine example of the literary style of the Renaissance. Although the writer's ideas on human morphology were Galenic, his metaphor was of Renaissance origin, that is, he looked upon the organism as a tower, a fortress, or a palace.

It would be interesting to consider how the historical moment was projected into the author's dream, for no idea blossoms forth on the spur of the moment without some backthread or forerunner in the human mind.[1]

In this sense, the dreams of Montaña de Monserrate revealed his concern—a reflection of the feeling of the times—in the problem of morphology, which at that time obsessed artists as well as anatomists, and his paradoxical method of wrapping the Galenist classic conception in such Renaissance clothing as the tower and the fortress forestalled the notions of Vesalius.

Other anatomists (Gimeno, Collado, Sánchez Valdés). Other anatomists of less renown were the already mentioned Pedro Gimeno, who studied at Louvain, Paris, and Padua with Vesalius and wrote *Dialogus de re medica* (Valencia, 1549); Luis Collado, who published a commentary on the Galenic work *De ossibus* (Valencia, 1555), and who defended Vesalius against Sylvius; and Juan Sánchez Valdés de la Plata, who wrote a general anthropology including a long chapter on anatomy.

Anatomists after Vesalius (Valverde). The second third of the sixteenth century is the Golden Age of Spanish anatomy, and during that period a number of great anatomists flourished. Among them Juan Valverde de Amusco stands out. He was a native of Palencia, took his general courses in philosophy and the humanities at the University of Valladolid, after which he went to Italy to study anatomy under the aegis of Realdo Colombo in Padua, and later at Pisa, being a witness of the revolution in concepts initiated by Vesalius.

The finest fruit of his anatomical studies was his work entitled *Historia de la composición del cuerpo humano* (History of the Composition of the Human Body), first published in Spanish in Salamanca in 1556, being widely read for practically a hun-

dred years. Pope Paul IV granted the license for its publication and imposed the penalty of excommunication and a fine of one hundred gold ducats on "anyone selling it without the author's permission."

After the first Spanish edition, two editions in Italian were published in Venice in 1560 and 1586, another in Flemish at Antwerp in 1568, and two others in Latin in 1589 and 1607.

In the bustling Renaissance atmosphere, Valverde could have bowed to the prestige of Galenist ideas and servilely adopted the classic view of Sylvius. He could also have allowed himself to be carried away by the whirlwind of Vesalius' personality when it struck Padua. Instead, because of his own forceful personality, Valverde adopted Vesalius' work only to submit it to a profound intellectual scrutiny, personally checking Vesalius' findings and rectifying his errors.

Valverde made no mere rehash of Vesalius' *Fabrica*, but conscientiously labored at remodeling the Vesalian monument. "Whom [Vesalius] I shall always follow in this history," said Valverde, "except in the order of description, in which he is slightly confusing (through not wishing to diverge from Galen) and in certain things in which verily he used less diligence than was properly due (perchance leaving off in the middle of a long labor), which things I shall deal with at their proper time. . . ." Therefore, Valverde corrected the order of description and improved the morphology of the *Fabrica;* on the basis of his great experience in dissection, he corrected many of Vesalius' errors and expounded clearly the minor circulatory system.

Valverde was therefore no plagiarist but a fit recreator of Vesalius' work. He described man as a building or a statue, and his anatomy was basically static. His text amended and completed Vesalius' work, and his anatomical illustrations were superior scientificomorphologically and artistically to those of the *Fabrica*, being founded upon his anatomicopathological necropsies and his wide clinical experience.[M]

In his *History*, Valverde introduced anatomical figures after the style of Vesalius but greatly improved upon them both artistically and in their exactness. He entrusted their execution to the Spanish painter Gaspar Becerra, who belonged to the schools of Alonso Berruguete and Michelangelo. One can clearly perceive the influence of the Italian master as one studies the magnificent plates. The general nature of the composition, the clean-cut relief, the effect of motion in the figures are characteristic of the art of Michelangelo. They are tense forms, overflowing with vitality and athletic energy.

In Vesalius' illustrations, the background of fine Italian landscapes animates and softens the whole, counteracting the doleful impression of skeletons and bodies in the raw. In Becerra's plates, the background of bare arid land, the jagged hills typical of the bleak wastelands of Castile, dramatizes the dissected bodies with their contorted muscles and limbs.[N]

Valverde pointed out in the explanations to his plates the corrections he had made of mistakes in Vesalius' *Fabrica*. He acknowledged withal the value of his predecessor's plates, as shown in the warning he gives the reader at the beginning of his *History:* "Although some of my friends," he said, "opined that I ought to make fresh drawings, instead of using Vesalius' I preferred not to do so in order to

avoid confusion, it not being known so easily how far I agree or disagree with him, and besides his drawings are so well made that it might have looked like illwill or envy had I not used them. In fact, it has been as easy for me to improve on them as it would have been difficult for anyone in disagreement with them to make new ones. But since mine are cut out on copper and cannot be inserted within the text of this History without a great deal of confusion, I have put at the end of each book those which belong specifically to it."

In the eulogy Valverde made of Vesalius' drawings, he pointed out as one further reason why he did not discard the illustrations of the *Fabrica* that in this way he was better able to show wherein he was at variance with them, thus indicating his belief of having done an original work.

It is of importance to point out that Valverde (who from his portraits appears to have been a gaunt, bearded, shrewd type of man) used Spanish in his writings with terms borrowed from the common vernacular.

The Renaissance witnessed the birth of national states. The great mass shiftings of population caused by the Crusades created an economic phenomenon that demanded the creation of new states. With political freedom, monetary economy, credit, bureaucracy, and a new social system made their appearance. National consciousness then sought footholds in local tongues, in opposition to the abstract internationality of Latin. The Renaissance dignified a vernacular language for political reasons, so that the language might be the first foundation stone of the legal structure of the new nations, and the new languages acquired decisive importance.

Vesalius' *Fabrica* was published in Latin because its author was saturated with the universalist unity of medieval Europe, which was being dismembered under the cudgeling of the Reform, and because he was dedicated to Charles V as the last representative of political unity in Europe; while Valverde on the other hand gave his work a purely vernacular style and spirit.[O]

Even if the sole merit of Valverde's work were no more than its rich, expressive Castilian language, that would still be sufficient to make it immortal.[P]

Artistic anatomy and ascetic anatomy (Arfe, Fray Luis de Granada). Two other famous Spaniards, not physicians, wrote about anatomy at this time. The first was Juan de Arfe y Villafañe, an artist in whose *Varia commensuración para la Pintura y Arquitectura (Variable Proportion for Painting and Architecture)* was contained a whole book on artistic anatomy.

Arfe, the "Spanish Cellini," belonged to a family of artists of Teutonic origin who had settled in Spain. A talented sculptor and goldsmith, his work graced many churches and cathedrals, including the famous monstrances of Avila, Valladolid, and Seville. After learning his craft under his father and grandfather and attending the anatomical expositions of Cosme de Medina, he wrote in his mature years the aforementioned work (Seville, 1585), which he dedicated to Pedro Girón, Duke of Osuna and Viceroy of Naples.

Arfe divided his work into four books: Book I, dealing with geometrical figures; Book II, dealing with the individual dimensions and proportions of the members of the human body, and their bones and arm muscles; Book III, dealing with the

statures of birds and beasts; Book IV, dealing with architecture and church ornaments.

Anatomy, therefore, was for this artist a subsidiary sphere of knowledge necessary for the perfection of his art.

The Spanish monk, Fray Luis de Granada, of the Order of Preachers, attained a fame as an orator that reached out to all the confines of the Iberian peninsula. In his last years he wrote a basic apology on faith, *Introducción al símbolo de la Fé (Introduction to the Symbol of Faith)*, a singular milestone in the ascetic literature of Spain.

According to Fray Luis, contemplation of the world instills a series of fundamental principles on the existence of God as the Arranger of created things that may be reduced to: arrangement of the cosmos or inanimate world; the marvelous organization of nature in the service of man; and the wonderful structure of man himself forming a lesser universe within him.

Fray Luis briefly described the anatomy of the organs, starting with the liver. Although he never mentioned them, he was probably aware of the works of Montaña de Monserrate and Lobera de Avila, particularly of their anatomical descriptions in the form of "dreams." These probably helped him to arrive at his comparison of the stomach and liver. The liver, he said, is "like the butler in a great household, who distributes the food and gives something to eat to all its members. If the stomach is the cook, the liver is the butler and the one who deals out everything." Fray Luis ended his work with a brilliant eulogy of the hands, "servants and ministers of reason and wisdom." His is probably the most remarkable work on ascetic anatomy ever written.

XII. THE SURGEONS

The meaning of Renaissance surgery. Renaissance surgery is an adventure in the etymological meaning of the word, as Lain Entralgo has commented. It is *ad ventura*, "come what may," risk, original insight, or technical mastery of things.

Some phases of history incite man to adventure. One of these was the Renaissance, when European man, coming out of the medieval age though not yet quite at the modern stage, felt himself at a turning point and sought adventure as a plain seaman, a conqueror, or a pirate. At their side stands the surgeon.

Two hitherto unknown concepts of reality were born in the Renaissance, according to one of which nature was a combination of geometric shapes, and according to the other the universe was made up of an organism of living forces and beings. Paradoxically enough, the chief work of the Renaissance was Vesalius' *Fabrica*, which is modern only in the dynamism of its anatomy and Galenist in its physiology.

The story of the new surgery, however, was in itself an adventure. The professional distance between physicians and surgeons was much greater in France, England, and Germany than in Spain and Italy. The growing importance of the post of hairdresser at the Royal Court placed all surgical activities in the hands of the barbers, or rather of the master barber. In the latter half of the seventeenth century, the barbers and surgeons joined forces *against* the "professional" physicians.

In England, "long-robe" surgeons strove against "short-robe" surgeons or barbers until well into the sixteenth century. Henry VIII, at the request of Thomas Vicary

(1495–1561), Barber-Surgeon to the King and writer of the first text of anatomy in English, brought the long-robe and short-robe surgeons all into one guild.

On the other hand, in Spain as in Italy chairs of surgery had already been established. Vesalius, Fallopius, and Fabricius ab Aquapendente were at once surgeons and anatomists. Francisco de Arceo depicted the academic surgeon as a lesser and empirical type of quack.

Firearms, which had recently been invented, posed fresh problems for the surgeon, and the new anatomy and its techniques made surgery a stimulating adventure.

Spanish surgeons of the Golden Age revised their treatment of old cold-steel wounds and new firearm wounds, and made advances in amputation, skull trepanation, ruptures, grafting and urological operations, obstetrics, and ophthalmology. The union of medicine and surgery was finally reached in Spain under the enlightened auspices of Ambroise Paré.

Fragoso, Arceo, Hidalgo de Agüero, Daza Chacón, López de León, Vigo. Juan Fragoso, a resident of Toledo and physician to the Royal Chambers of Philip II, was a classic surgeon with wide experience gathered on the battlefields of Europe. Among other treatises, he wrote an excellent *Cirugía Universal* (*Universal Surgery*) (Alcala, 1601), containing many a contribution to forensic medicine and references to the ligature of arteries and the treatment of aneurysms.

Fragoso defended the mercurial treatment of syphilis as against fumigations recommended by Agüero. He practiced intestinal suture. He became the father of Spanish forensic medicine with his *Second Treatise on the Statements to be Made by Surgeons Regarding Various Illnesses and Many Ways in Which Death May Customarily Take Place*, which to this day would well serve as a guide to surgeons in the formulation of legal opinions as to possible causes of death.

Born at El Fresno (1493), Francisco de Arceo studied at Alcalá de Henares, and was physician to the monastery of Guadalupe (Spain), attending surgical patients from even France and England. He was a fellow-student and intimate friend of the noted theologian Arias Montano, who edited one of Arceo's surgical treatises. Arceo continued to perform operations with success even in his eighties.

In 1574 Arceo published at Antwerp his *de Recata vulnerum curandorum curatione*, written in Latin so that only the truly learned physicians might make use of it. His basic surgery principles were simplicity, cleanliness, and humility. His *Treatise on Wounds and Their Healing*, translated into English, Dutch, and German, covered forty-five years of practical experience. Arceo developed a balm that bears his name and a method of rhinoplasty antedating that of Tagliacozzi.

Andrés Alcazar, of Guadalupe, invented an apparatus for draining the fluids from carbuncles.

Juan Calvo, a graduate of Zaragoza and professor of medicine at Valencia, established a surgical academy in his own house and published textbooks on surgery, syphilis, and internal medicine.

The first surgeon in Spain to teach first aid for wounds was Bartolomé Hidalgo de Agüero (1530–1597), who was born and educated at Seville. His so-called *Tesoro* is the first Spanish treatise on the human eye. He was aware that the "dry cure" was a roundabout method in the treatment of wounded and traumatic cases, which,

prior to Agüero, had an eighty per cent mortality rate. His axiom "interfere the least possible with a wound" is the basis of modern traumatology.

The Spanish venerated him as a god and whenever they became involved in a fight, they would say: "*En Dios me encomiendo y en las manos de Agüero*" (In God I trust and in the hands of Agüero). He was the Spanish Ambroise Paré and, like Paré, did not believe in the value of suppuration.[9]

Agüero was, moreover, a forerunner of medical statistics when he stated that "in the past year, 1573, four hundred thirty-six cases entered the hospital and twenty died, and in two and a half months in which head wounds were recorded separately, fifty-seven came in and only seven died, and during the years in which I and my predecessors have practiced cures in the common way, the number of deaths was less than the number of survivors."

The humanitarian surgeon Dionisio Daza Chacón (1503-1596) was born in Valladolid, studied philosophy there and surgery at Salamanca, and was an army physician during the wars of Charles V and in the fleet of Don Juan de Austria at Lepanto. It is said that on that "the most memorable occasion to be seen for centuries" he treated the wounds of a soldier called Cervantes. A precursor of vascular surgery, he rejected the boiling oil treatment of wounds, and was the first to recommend ligature of the tumor in the treatment of nasal polyps.

A true Castilian, he lived for more than eighty years and was both soldier and courtier during two great reigns. He was a conservative surgeon and a merciful one, devoting time and attention to both the victims of the executioner and the wretched slaves on the king's galleys. A great faultfinder among his colleagues and a glutton for globe-trotting, he was greatly mortified when he was pensioned off on his seventieth birthday. After this enforced retirement, he wrote *Practice and Theory of Surgery*, etc (Valladolid, 1609).

Daza Chacón disagreed with Vesalius regarding the cure of the heir apparent, Don Carlos. Vesalius thought that the abscesses and erysipelas from which Philip II's son suffered were affecting "the clothes" (the meninges) and he advised trepanation. Daza Chacón held that the meninges were not affected, basing his opinion on the patient's very slight symptoms. Trepanation was performed, being started by Vesalius and finished by Daza Chacón, upon the orders of the Duke of Alba. During the operation no pus was observed below the cranium. Many participated in the consultation, with the King seated in the middle, and there was great flaunting of medical erudition by all parties concerned.

As affirmed by Daza Chacón in one of his writings, the Spanish and Flemish physicians "killed" Don Juan de Austria, the hero of Lepanto, when they lanced his hemorrhoids and bled him to death. Daza Chacón said that he "would have used leeches." "Had I been present," he added, "such a mistake would not have been made."

Daza Chacón had much military experience. He commenced his military practice under the orders of one of Charles V's surgeons, and ultimately participated in all the Mediterranean campaigns of Don Juan de Austria aboard the Spanish galleys. In the removal of nasal polyps he used injections of sour pomegranate juice as a cicatrizing agent.

The reputation of Pedro López de León extended from Seville in Spain to Cartagena in Colombia, where he practiced and published a treatise on surgery containing a description of the treatment of aneurysms and the application of the methods devised by his master, Agüero.

One of the greatest Spanish authorities on surgery in the seventeenth century was Juan de Vigo, who rose to the position of physician to Pope Julius II. He wrote *Técnica práctica en cirugía* (Technique and Practice of Surgery) (Perpignan, 1627), referring to internal illnesses, particularly gout.

Sickness and death on the royal galleys. Medical practice on the galleys of Philip II has been brilliantly described by Marañón, whose work should be consulted in any study of Spanish surgery in the times of Don Quixote.

The galley was an oar-propelled vessel symbolizing will power, against the sail-propelled vessel symbolizing chance. The galleys were floating hells oar-driven by slaves chained together and lashed to their seats, their sore-infested backs bent under the flogging of the whips applied incessantly by the brutal gangmasters. The gyves were removed from their feet only upon death, and often they had to endure the howls and ravings of the last agonies of their dying companions.

They slept in the open with nothing more than a sackcloth, exposed to the rain, the sun, and extremes of cold and heat, rowing without surcease, the *anguila* or whip-lash forever playing on their backs, days upon days, without a moment's respite.

Their diet consisted of hardtack, that is, half-fermented bran bread baked twice in order to eliminate the moisture, which made it so hard that it was necessary to soak it in sea water and even then the teeth stuck into it at the first bite and were torn from gums softened by the scurvy with which all galley slaves were afflicted. To the piece of hardtack, a mash of *habas* or dried beans boiled in plain water was added once a day. On rare occasions a little oil, vinegar, or wine was added. With the leavings of hardtack a miserable soup called *mazmorra* was concocted and served at night. Weevils and mold frequently rendered the food and water unfit for consumption. Filth, excreta, vermin, rats—this was the environment of the unfortunates condemned to the galley chains.

Punishments included starvation diet, flogging, amputation of nose and ears, and quartering of the convict by four galleys. Galley sentences were usually limited to a year or two, since any longer was—as Don Quixote said—"living death"; but lack of men for the oars caused sentence to be passed on ordinary vagrants, on poor souls who "stole ten ducats," as is mentioned in *Don Quixote*, and on gypsies.

The most frequent diseases in the galleys were avitaminosis, rickets, scurvy, beriberi, pellagra, enteritis, and infections. Medical attention was in the hands of barbers and "wound surgeons" who bought their diplomas for four gold escudos. Galley slaves were sometimes attended at port hospitals such as Santa María and Cartagena in Colombia. On important naval expeditions, court physicians, such as Lobera de Avila or Perez de Herrera, accompanied the fleet. These positions preceded appointment to the coveted post of personal physician to His Majesty. Amputations were done by hot iron, scraping knife, and saw, while the galley slave bit on a rag clenched between his teeth. Medical treatment was elementary if not entirely lacking.

López Madera and Daza Chacón, as previously mentioned, were physicians on the flagship at Lepanto. Daza Chacón was well acquainted with hackbut wounds and did not customarily extract the bullet unless it happened to have lodged in some vital organ. Instead of using white-hot iron for amputations and to stop bleeding, Daza Chacón used bandages, effecting the final healing with a mixture of egg whites, dragon's blood, Armenian bole, and aloe. In cases of the cutting off of a hand, a common punishment for thieves, Daza Chacón first stretched the skin upward, bound the arm tightly where the skin had been stretched, and drew the line for the ax blow; later he covered the stump with the retracted skin, sewed the skin edges together, and then plunged the stump into the belly of a live chicken in order to prevent hemorrhage.

Twenty-five thousand Turks and eight hundred Christians died at Lepanto. Cervantes was among the fighting Christian soldiers and was very likely treated for an arm wound by Daza Chacón. Only during battle did wounded galley slaves receive medical attention and a double ration of vegetables, white bread, and wine.

The galleys and their human drama were indeed the dark side to the glittering story of the Spanish conquests in the times of Don Quixote.

XIII. NOSOLOGISTS AND EPIDEMIOLOGISTS (VILLALOBOS, VALLES, MERCADO, TORO, PORCELL)

At a time when infection, besides death in armed combat, was the most frequent cause of death, it is logical that epidemiology was more important than it is today when, thanks to antibiotics and chemotherapeutics, it promises to become a preventive science.

In the Spain of Don Quixote, "the plague," as all contagions were then called, was the subject of special attention by physicians.

The first book on medicine printed in Spain—and this fact is of utmost significance—was the *Tratado de epidemias y pestes* (*Treatise on Epidemics and Plagues*), by Velasco de Taranta, translated into Spanish by Juan Villa (Barcelona, 1475). Ten years later came *Medicinas preservativas y curativas de la pestilencia* (*Healing and Preventive Medicines Against Pestilence*), by Diego de Torres (Salamanca, 1485), which was the starting point for the epidemiological literature of the following century.

Although all the physicians of that period were nosologists and epidemiologists from sheer necessity, the most outstanding among them were Villalobos, Valles, Mercado, Toro, Porcell, Lobera, and Laguna. The last two will be discussed under another heading.

Francisco López de Villalobos, a native of Old Castile, probably from Zamora and perhaps of Jewish blood, was born in 1473 and lived in the glorious epoch between the end of the fifteenth century and the beginning of the sixteenth, when an extraordinary queen performed the feat of lifting Spain back on its feet. A born builder possessed of great vision and a miraculous faith, Isabella the Catholic erected the sturdy political scaffold that provided Spain with a new glowing façade of glory.

Villalobos was physician at three great courts: Ferdinand and Isabella's, Charles V's, and Philip II's, being present as personal physician at the deaths of both Ferdi-

nand and Isabella. He wrote scientific treatises of the highest order, particularly a *Sumario de medicina en uso mayor y Tratado sobre las pestíferas bubas* (*Summary of Medicine in General Usage and Treatise on Pestilential Buboes*) (Salamanca, 1498). He was a poet, an astrologer and an astronomer. One of his works bore the extraordinary title *Book of Problems Dealing with Natural Bodies and Ethics and Two Logbooks on Medicine; the Treatise of the Big Three: Babbling, Buffoonery and Brangling; with a Song and an Amphitrion's Feast* (Zamora, 1543).

When he was near the end of his life, Villalobos joined the Franciscan order. Humorist, skeptic, and master of the Castilian language, Villalobos became famous for his work in verse entitled "Dr. Villalobos on the Contagious and Accursed Buboes. Their history and medication" (Salamanca, 1498).

The most famous practitioner of his times in Spain was Francisco Valles (1520–1592), a native of Covarrubias, near Burgos, who obtained his doctorate at the University of Alcalá where he afterwards taught. Through his erudition and knowledge he became known as the Spanish Galen. He published many versions of and commentaries on Hippocrates, Aristotle, and Galen, became Court Physician of Castile, and standardized the requisites for securing medical degrees and licenses.

Valles was a great commentator of Galenic tradition and mentality and a pioneer of pathological anatomy. Boerhaave, speaking of Valles' commentaries on Hippocrates, said that "if one believed in the transmigration of souls, then Valles was the reincarnation of Hippocrates himself."

Valles anticipated Bacon in proclaiming the excellencies of the experimental method, and he was a "Cartesian" even before Descartes since he advised methodical skepticism as a method of trial and error, advice that he stressed in his medicoanthropological exegesis of the Bible (Lyons, 1588) entitled *De iis quae scripta sunt physice in libris sacris, sive de Sacra Philosophia liber singularis*. As a reward for this work, Philip II appointed him, together with Ambrosio Morales and Arias Montano, to organize the Escorial library.

Valles assuaged the gout pains of Philip II with tepid water footbaths. Grateful for the relief thus afforded, Philip II bestowed upon him the title of "El Divino." It was to Valles that the tragic and beautiful one-eyed Princess of Eboli, confined for life by order of Philip II for complicity in the murder of the Duke of Escobedo, appealed without success to certify that her health depended on her liberty being restored.

Of his many works, we mention as worthy of distinction the *Comentarii de urinis pulsibus et fe bribus* (Alcalá, 1565) and the *Methodus medendi Francisci Valesii* (Madrid, 1588).[B]

Valles' portrait shows him as a man of noble countenance, with that expression of skepticism and melancholic cynicism worn by the greatest spirits of the at once melancholy and merry, mundane and monkish, epoch of the Golden Age.

More versed than Valles in clinical practice was Luis Mercado (Valladolid, 1520–1606), personal physician to Philip II and Philip III, and teacher of Avicenna's Canon of Medicine at Valladolid.

Looked upon as the Saint Thomas of Spanish medicine because of his predilection for the scholastic style, Mercado was as classical in his content as he was Renais-

sance in the clearness and balance of his writing. He was Physician to the King's Council and Auditor of the Treasury. Among his works, his *Institutiones medicae* stands out. He inquired especially into intermittent and malignant fevers, women's complaints, and diseases of the liver, spleen, kidneys, and bladder. In his work *de Veritate et reta ratione principiorum, theorematum et rerum omnium ad medicam facultatum spetantium* (1604) he showed himself to be a philosopher of the highest rank. For the curing of gout he advised lukewarm baths and a minimum of opium, cupping, and purges, thus ranging himself against the bloodletting "vampirism" of the times. He was the first Spanish physician to describe the "garrotillo" or agranulocytic angina, recommending that it be treated with copper salts and boiling gold caustics, a method immortalized later in Goya's famous painting "El garrotillo."[8]

Together with Antonio Pérez, physician to Philip II and to Don Juan de Austria in his final illness in the Netherlands, and Luis de Toro (Palencia, 1522), who gave a description of the Great Plague (exanthematous typhus)[1] that scourged Spain from 1557 to 1572 probably in its second epidemic wave, there having been a previous one during the siege of Granada by Ferdinand and Isabella, we must mention Juan Tomas Porcell from Sardinia (which at that time belonged to Spain), who was famous for his bravery as well as for his scientific curiosity, which in the famous plague of Saragossa in May 1564 moved him to perform autopsies on five of the ten thousand victims of the epidemic, thus ascertaining that it was the bubonic plague.[4]

Porcell was the greatest Spanish epidemiologist in the sixteenth century and the originator of medical statistics. He once wrote: "I carried about with me my large notebook, divided alphabetically, in which I noted down details about those who had succumbed and how many days elapsed in the sickness and the opening (of the abscesses), or if they had died through their having burst prematurely, and why and how this had occurred . . . and everything else that was necessary."

XIV. THE "SPECIALISTS": PEDIATRISTS, OBSTETRICIANS AND GYNECOLOGISTS, UROLOGISTS, PSYCHIATRISTS, AND HERBALISTS (SORIANO, VELÁZQUEZ, CHIRINO, ACOSTA, CARBÓN, VALDÉS, DÍAZ, LEIVA Y AGUILAR, PÉREZ DE HERRERA, VEGA, HERNÁNDEZ)

The roll of physicians specialized in certain branches of medicine was so very long that we shall mention only a few as part of the main tableau of medical practice in the Golden Age of Spain.

Jerónimo Soriano, born in Teruel in 1575, so worthy and good that he was called "San Jerónimo," published a remarkable work on children's illnesses, the *Mejor modo y orden de curar las enfermedades de los niños* (Saragossa, 1600), which is one of the first treatises on pediatrics in the world.

A contemporary of the great Huarte of San Juan was Andrés Velázquez, who published *Libro de la melancolia* (*Book of Melancholy*) (Seville, 1585), of great psychiatric interest.

Alfonso Chirino published *Menor daño de la medicina* . . ., wherein we may note the curious mixture of superstition, magic, empiricism, and rudimentary science that characterized the therapeutics of Spain in the Golden Age.

Nicolás Monardes (1493–1588), a Sevillian and a brilliant business man besides being a physician and herbalist, published two famous works, one dealing with "everything brought from our Western Indies" (Seville, 1565), and the other entitled *Treatise on the Effect of Various Herbs* (Seville, 1571), whereby he imparted considerable impetus to the application of medicinal herbs. In another article[v] I have written about Monardes' botanical garden, where among other curative plants from the Indies he cultivated curare and tobacco.

Cristóbal de Acosta, nicknamed "the African," was a Portuguese settled in Spain who wrote in Castilian and published *Tratado de las drogas y medicinas de las Indias Orientales* (*Treatise on Drugs and Medicines from the West Indies*) (Burgos, 1578).

Besides to botanists, naturalists, and mathematicians of standing, credit must be accorded to those friars devoted to the study of medicine, such as Friar Bernardino of Laredo (1542), a Franciscan of Seville; Friar Agustín Farián, a Sevillian who practiced in Mexico; Pedro Barba of Valladolid (1541), who investigated the effect of cinchona; and the Benedictine Pedro Ponce de León (1520–1584), who conceived an original method of teaching deaf mutes.

The Majorcan, Damián Carbón, published *Libro del arte de los curadores . . .* (*Book on the Healers' Art*) (Majorca, 1541), one of the first treatises written on obstetrics.

Benito Daza Valdés published his *Uso de los anteojos* (*Use of Eyeglasses*) (Seville, 1623), in which lenses were described for the first time.

Francisco Díaz, physician to Philip III, published (Madrid, 1588) *Treatise . . . on all Diseases of the Kidneys, Bladder and Fleshy Growths in the Penis and Urinary Tract*, wherein he expounded his method of urethral catheterism, praised in sonnets by both Lope de Vega and Cervantes, which throws an intimate and revealing light upon the secret medical history of these two writers. He described the "Spanish operation" of lithotomy, and originated the first medical specialty in Spain.

Francisco Leiva y Aguilar published a book on the wrong use of tobacco entitled *Desgano contra el mal uso del tabaco* (Cordova, 1634), which was typical of the florid literary style of the period.

The Salamancan, Cristobal Pérez de Herrera, established in Madrid, with the aid of Philip II, the great asylum for the poor which later became the general hospital. He was both physician and soldier. His works appeared in the seventeenth century. He published one book in which he advised the use of "bland" remedies against epidemic "garrotillo" or diphtheria rather than painful cauterization with sulfuric acid, which was then the customary cure. He recommended "shaving the bulls," since three hundred people died in one year alone "on the bulls' horns." He was the archetype of the medical and humanistic adventurers of the sixteenth century. As attending physician on the galleys, he devoted many years to alleviating the lot of the poor, and in his immortal book *Discourse on the Protection of Real and Pretended Poor and on the Establishment of Housing in These Kingdoms and the Shelter of the Soldiery Pertaining Thereto* (Madrid, 1598) he studied the then appalling problems of the poor.

The poor were numerous due partly to the rapidly improvised social structure of Spain, which gave rise to a fearful misery side by side with magnificent institutions, and partly to the great number of vagrants who followed begging as a profession

and thrived in the shadow of that grandiose but disorganized social structure. The boundary between true and false beggars was difficult to establish because of the Spanish love for a vagabond life, which suited their lack of discipline, their love of freedom, and their few material needs. Perhaps the age-old habit of religious pilgrimages had intensified the desire to wander under the shelter of a mythical prestige and organized charity along the wayside.

The joy of Don Quixote and Sancho Panza on abandoning the soft luxurious life in the palace of the Dukes and finding themselves, without food or shelter but with their freedom, marching on the open road, is one of the truest literary symbols of the psychology of the Spaniard.

Cristóbal de Vega, physician to the Royal Chambers of Don Carlos, was perhaps the first Spanish psychiatrist, and in his works, published in 1576, there are detailed descriptions of melancholy and certain maniacal affections.[W] Spain at that time was far above the rest of Europe in the care of the insane, there being an insane asylum in Valencia as far back as 1409.

Francisco Hernández, physician to the Royal Chambers of Philip II, made a survey at the King's behest through New Spain, now Mexico, during which he studied the curative action of Mexican plants in the hospitals established by the Spaniards and tried out the effects of medicinal plants upon his own person. He was one of the foremost scientists Spain has produced. On his return to the Peninsula, he produced a twenty-six volume work.

The materia medica of the New World was described by Diego Alvárez de Chanca, who accompanied Columbus on his second voyage.

Considerable botanical research was carried out on the plants of the New World, and among the more famous botanists we may mention Gonzalo Fernández de Oviedo, García de Orta, and José de Acosta, as well as the aforementioned Francisco Hernández.

Travelers returning from America and the East Indies introduced quinine and four types of sudorifics: guaiacum, sarsaparilla, cinchona, and sassafras.

XV. THE HUMANISTS (LAGUNA, LOBERA DE AVILA, SERVETUS, PEREIRA, SABUCO DE NANTES, HUARTE DE SAN JUAN, SÁNCHEZ)

The philosopher-humanist-physician represented Spain's greatest claim to glory in the Golden Age.

Medical humanism originated with Boccaccio and Petrarch in the fourteenth century, the word "humanism" deriving from Cicero's *humanitas* and from Dante's "humanistic spirit," interpreted by Ariosto in the sense of Terence's *homo sum; nihil humani a me alienum puto*.

Humanism was born out of Europe's dissatisfaction with its immediate past and present conditions, and from the general pining for the good old days then revived in three forms: the translations of ancient literature by *philologist-physicians*, the instructive exposition of knowledge by *humanist-physicians*, and the philosophical commentaries by *philosopher-physicians*.

Among the humanists we shall consider the seven greatest, all of them spiritual

heirs and successors of Juan Luis Vives: Andrés Laguna, Luis Lobera de Avila, Michael Servetus, Gómez Pereira, Miguel Sabuco de Nantes, Huarte de San Juan, and Francisco Sánchez. These are the greatest medical humanists of the Golden Age of Spain.[X]

Andrés Laguna (1499–1560), a native of Segovia, was a redoubtable humanist, Hellenist, polygrapher, traveler, translator, and philosopher. He studied at Salamanca and Paris under Sylvius and at Padua with Colombo, and taught in the universities of Paris, Alcala, Toledo, and Bologna. He was physician to Charles V, whom he accompanied on his campaigns through Italy and Germany, to Popes Paul II and Julius II, and to Philip II, executing many religious and diplomatic missions in Europe. Laguna was one of the first great Spanish physicians of universal repute, and he belongs in the honored company of Villanova and Servetus.

Famed at the Spanish Court, Laguna spent many years traveling all over Europe in attendance on royalty and in the retinues of great personages. He had the pride of his class and the awareness of his mission; and he let fly without mercy at those unqualified people who presumed to lift the veil of mystery surrounding the human being.

His work *Anatomica Methodus, seu de sectione humani corporis contemplatio* (Paris, 1535) was representative of the anti-Vesalian phase of Spanish anatomy, which was still drawing its nourishment from medieval learning. His treatise, a short text of some seventy pages, included a dedicatory epistle to the Bishop of Segovia, his father's patron and protector. His anatomy started with the mouth, "where food undergoes the first process of digestion," and ended with the brain, "where the final and most absolute transformation of the mind takes place."

Laguna also published a treatise on the plague entitled *Short Discourse on the Curing of and Preservation from the Plague* (Salamanca, 1546), wherein he put forward his mercurial friction treatment, dietary rules for impoverished students, and a critical commentary on Galen.

In his *Enfermedades de las articulaciones* (*Diseases of the Joints*), he described a method of treating ulcerous arthritis or suppurating tophi in the secreting stage with poultices of lard and fermenting cheese (*caseī ad modum inveteratum*), thus anticipating by four hundred years the empiric use of penicillin for the treatment of infections.

He investigated the dispersion of pollen and plant physiology and was a noted botanist, making a particular study of sassafras, guaiacum, and sarsaparilla.

Laguna was called upon to control and study the plagues that decimated the cities of Antwerp and Metz. He attended patients of the highest rank, including Queen Elizabeth, together with Villalobos, though in this case he was unsuccessful. He created the first botanical gardens in Spain, at Aranjuez, the idea coming to him from his botanical studies at Cologne. He contrived an apparatus for turning sea water into drinking water; and made an excellent translation of Dioscorides.

In his famous political speech solemnly delivered at Cologne in 1543 under the title *Europa sese discrutians*, he spoke with deliberate pessimism regarding the breaking up and death of nations on the continent and the mortal danger of their internecine warfare to the future peace of Europe.

Laguna's bones are preserved at Segovia, enclosed in a modest wicker hamper.

Luis Lobera de Avila was born sometime between the 1470's and the end of the century. His main work appeared in November 1551. He was a follower of Galen, and accompanied Charles V on his warring campaigns. He studied at Salamanca and other European universities, and was active as physician and traveler through Europe and Africa with the Emperor's armies. He wrote commentaries on the classics (Aristotle, Hippocrates, Galen, and Avicenna) and produced much work on anatomy, plague, and syphilis. We may mention here his *Banquet of Noble Knights and Rules for Living from the Time of Rising until That of Retiring* (1530); *Garden of Health* or *Gentlemen's Banquet* (Alcalá, 1542); *With Two Treatises on Spanish Travels by Land or Sea* ("*Precepts on the Sea*" and "*Precepts for Land Travelers*"); and *Book on the Four Genteel Diseases, Namely: Catarrh and Gout; Arthritis; Gallstones, Renal Calculus and Colic; and Buboes* (Toledo, 1544).

Michael Servetus (1511–1553), whose home town was Villanueva de Sijena in the province of Huesca, studied the humanities at Saragossa and law at Toulouse, and upon reading the free commentators on the Bible lost his Catholic faith. He took refuge at Basle and Strasbourg, leading a lonesome and tormented existence, writing his *de Trinitatis erroribus* (1531), which resulted in his being expelled from all reform churches.

Setting up at Lyons under the name of Michel de Villeneuve, he studied medicine in Paris as a pupil of Fernel and a classmate of Vesalius, assailing the Arabian system of using sirups in his *Syruporum universa ratio* (Paris, 1537). He resided afterwards in Lyons, Charlieu, and Vienne (Dauphiné), practicing as a physician for several years, but led away by his zeal for religious reform, he undertook a ridiculous exchange of polemics with Calvin, the theological dictator of Geneva. In 1553, Servetus clandestinely published his *Christianismi restitutio*. Arraigned by the Catholic authorities of Vienne, he was imprisoned but escaped. Victim, however, of his obsession, he went to Geneva, where he was subjected to a lengthy trial and, in October 1553, at Calvin's command, was burnt alive slowly over green wood.

Though Galen had mentioned the passage of blood from the pulmonary artery to the pulmonary vein, Servetus was the first to describe the lesser or pulmonary circulation, even *prior* to Valverde and Colombo. His was an anatomical and theological physiology. In his writings genial intuition was mingled with secret experimentation, but his mentality was still of the Galenic school. Servetus was the martyr of Spanish free thought, a Quixote in ideas who never attained his Dulcinea of fame.

Antonio Gómez Pereira, born in Medina del Campo in 1500, a Jewish philosopher and physician to the royal chambers of Philip II, was one of the doctors attending the prince Don Carlos in his final illness, when that illustrious patient, suffering probably from catatonic schizophrenia alternating with bulimy and negativism, was seized by a gastroenteritis aggravated by a purge that brought on a choleriform syndrome

Long before Sydenham and in opposition to the school of Galen, Pereira established the value of fever as an expression of nature's effort to restore normality, and he identified body heat with fever heat. He had patients from all over Spain, in Burgos, Segovia, and Castile.

His famous work *Antoniana-Margarita opus nempe physicis, medicis ad theologis non*

minus utile quam necessarium (Medina del Campo, 1554), the name of which is a tribute to his parents Anthony and Margaret, was a reasoned revolt against the tyranny of the doctrines of Aristotle and Galen, which formed the basis of the medical dogmatism ruling at the time. Fanatical Galenists nearly destroyed the whole of this work.

Pereira belongs to the same great tradition as Luis Vives, Raymon Lull, and Suarez on the one hand, and Seneca, Averroës, and Maimonides on the other. A born enemy of the authoritarian principle in science, in physical matters he accepted only the sanction of experience. Endowed with considerable dialectic force, he was the champion of the anti-Galen school and of direct observation of nature. He was a century ahead of Descartes in his rationalistic concept of life. In his book, he expounds the original idea of automatism or involuntary action in animals, later amplified by Descartes. On the question of the immortality of the soul, he adduced, before Descartes was even born, the Cartesian proof based on the dualism of humanity.

In experimental psychology in his time he was more advanced than either Bacon or Descartes were later. He denied that animals could feel, since if they had feelings they would have to form judgments and he held them to be no more than machines. He was the originator of the syllogism, "I know that I know something. Everyone who knows *is;* hence, I am."

Miguel Sabuco de Nantes had a daughter "endowed from head to foot," in the words of her contemporary Sotomayor, "with a thousand divine gifts." Sabuco de Nantes published, under his daughter's name, a passionate, intuitive, long-winded, and arbitrary book, dedicated to Philip II, entitled *Nueva filosofía de la naturaleza del hombre no conocida ni alcanzada de los filósofos antiguos* (*New Philosophy on the Nature of Man, Unknown and Unattained by the Old Philosophers*), in which the classic dogmas of the past were vigorously attacked.

Sabuco promulgated the theory of a "cerebral or neural juice" which it has been believed was an intuitive anticipation of the cerebrospinal fluid, or a harbinger of the basic role that is given nowadays in the vegetative and affective life to the diencephalon area and the adjoining pituitary gland, i.e., the hypothalamic-pituitary system. Here are his own words: "The cause and factory of every disease is the brain; there the emotions, passions and motions of the mind have their seat; there feeling or sensation is rooted; there lies the root and nature that causes vegetation; there life and cravings spring from; there disease originates; and there death comes from." We should note that he attributed "vegetation," i.e., origin and control of vegetative life, to the diencephalon.

The cause of disease was to Sabuco "the drawing or flow of moisture from the brain, damaging the parts where it stops; or cessation of the functions of the brain."

Juan de Dios Huarte y Navarro (1529–1589) studied medicine at the University of Huesca, where he obtained his diploma upon writing his *Examen de ingenios para las ciencias*, in 1557, of which Marañón has said: "If I were to be asked what is the most important work on medicine in Spain up to the eighteenth century, the work most worthy of being placed permanently in the great bibliography of the universe, I should answer without hesitation that it is this one, the only book written by a humble doctor born in a village, San Juan de Pié de Puerto in Navarre, who studied

in a provincial university, the University of Huesca, who practiced in sundry places of Spain, and who was far from all academic and official honors and posts."

Starting with Galen's *de Temperamentis*, Huarte made his way through the works of the physiognomists and established the basis for subsequent phrenological, constitutional, and psychosomatic studies. His treatise is a splendid instructive psychology, a perspicacious and clever work that establishes connections between the ethical and the physical, and shows how the cranial and cerebral structures affect the professional aptitudes of every individual. The natural temperament of a man, Huarte claimed, is what predisposes him for the exercise of a particular technical or intellectual activity. Thus Huarte originated the theory of professional aptitude. Huarte established the thesis of the native equality of spirits and the correlation of temperament and talent, denying the effects of apprenticeship, habit, and vocation on intellectual aptitude and efficiency. On this subject of aptitude, he also took into account such features as the hair, the smile, and temperament and ingenuity.

This genius of a man, reared at the foot of the age-old oaks of Roncesvalles, wrote a singular book from which despite his protestations of orthodoxy the Holy Office deleted several pages. As against the professional guidance practiced today, Huarte recommended the "investigation of aptitude"; as against today's technical aptitude, he advised personal inclinations and vocation, that is, enthusiasm for the job chosen, a sincere and efficient enthusiasm. Huarte recommended that instruction be preceded by university training of the teachers, without which teaching is like "drawing water into a basket."

Francisco Sánchez (1551–1623), literary forerunner of Montaigne, of Jewish descent, was born in Braga and studied medicine in France and Italy, becoming a professor at Montpellier where he had graduated at twenty-four years of age, practicing subsequently at Toulouse. Like Juan Luis Vives, Sánchez was a standard-bearer of sixteenth century Spanish skepticism and criticism. A skeptic regarding the science of his age, he started a rebellion with his medical works, his commentaries on Galen and Hippocrates, and his philosophical writings. In his famous book *de Multum nobili et prima universali scientia, quod nihil scitur* (*On Many Worthy Universal Principles of Science of Which Nothing is Known*), written in 1576 and published in 1618, he displayed his enthusiasm for the physical sciences and natural philosophy, and formulated the methodical questioning that is the basis of Cartesian philosophy some sixty years before the *Discours de la méthode* made its appearance.

He based his philosophy on the dissections he was able to perform as a member of a secret society in Toulouse which provided him the corpses. It was his idea that metaphysics had to give way to the experimental science that studies all phenomena according to a scientific criterion. He was a nominalist in opposition to the essentialists. "Our philosophy," he said, "is a Cretan labyrinth in which it is impossible to avoid the Minotaur."[X]

EPILOGUE

Spanish medicine, as Spain itself, in the Golden Age was a vast multicolored tapestry woven out of passionate contradictions. If Spanish individualism hampered the

progress of scientific research, on the other hand encyclopedism, humanism, and the avid curiosity of the physicians widened the clinical horizon of medicine and speeded its progress.

The yearning to explore new worlds was also translated into the urge to unveil the mysteries of the human body, thereby stimulating anatomy. The endless wars and military campaigns fostered the progress of surgery and traumatology, and forced medical attention to focus on epidemiology and nosology, as "fevers" and "the plague" were national scourges. The national diseases—gout, *garrotillo*, urinary tract stones, and *tabardillo*—also spurred the study and treatment of these diseases.

But the greatest glory of the Spain of the Golden Age were its humanist-physicians, who integrated science and conscience, thought and belief, medicine and philosophy, scientific spirit and professional humanitarianism. These men performed feats in psychiatry and medical philosophy, and they established the foundation upon which it would be possible to build the future Spanish medicine.

They made ideals of to serve and to heal. Their dedication to these ideals is the proudest heritage handed down by that passionately quixotic country which was the Spain of Don Quixote.

NOTES

A. The great epoch of tolerance extended from Juan de Valdés to Michael Servetus, whose last words on being burned at a green wood stake in Geneva were, "Mercy! Oh Lord! Mercy!"—noble words full of pleading, not to the Trinitarian clemency of Calvin, but to the concept of the Supreme Being. After the burning of Servetus by Calvin's henchmen, the followers of Erasmus gathered around the remarkable figure of Sebastian Castello Castigliani and issued the first European proclamation regarding tolerance.

B. In chapter 17 of *Don Quixote* the peccancy of Spain at that at once grandiose and miserable moment of her history is described with a keen, almost clinical, eye.

C. One device of the favorite, the Duke of Lerma, who thought he had found a universal panacea against inflation, was to raise the value of the currency in order to make good the difficulties of the exchequer and turn all Spaniards from poor to rich! This madness was symbolized in the cure-all panacea or balm of Fierabras described in *Don Quixote*.

D. The first polyglot Bible in the world was published in 1514 at the Theological University of Alcalá, complete with critical and grammatical appendix and glossary, being probably "the first scientific work printed in the civilized world."

E. Spain took enthusiastically to the art of printing. The first Spanish book was printed at Valladolid in 1464. Up to the end of the fifteenth century, seven hundred twenty books were printed in twenty-five Spanish cities, as against three hundred fifty-eight books printed in England. Because of the world-wide importance of Spanish at that time, books were printed in that language as well as in Latin.

F. Though the "Black Legend" was not historically justified, we must on the other hand recognize that the Spaniards of yore, just like their descendants today, possessed a racial tendency toward violence and theatricality, exaggerated then by the feeling that they were the leaders on the universal stage of history, with the whole world hanging breathless upon their actions and pronouncements.

G. Though art is a flower capable of blossoming on the sterile ground of poverty, science requires wealth and well-being as well as a universal idiom. The arts have their own language, namely, melody, color, rhythm, or harmonious shape. Science on the other hand requires a linguistic instrument with which to raze all barriers and guarantee itself an indispensable universality. All discoveries become universal as soon as made. The laws of gravity, the refraction of light, the microbial origin of infection, vaccination—all these discoveries became universal from the very moment they were announced.

H. Individualism, because it goes hand in hand with a spirit of rebellion, has often given birth to artistic genius or has accompanied it, but it has always been a stumbling block to scientific progress.

Individualism frequently embraces encyclopedism, as occurred among the physicians of the Golden Age, each of whom individually presumed to embrace the whole of the scientific knowledge of his time.

Science, however, advances only by teamwork, which is the same as saying the proper combination of specialized labors. Science, except for cases of geniuses who by intuition make great advances in a scientific field, requires teams, that is to say, specialization instead of individual encyclopedism, which is the best grounding for the arts.

I. While in Spain quackery was being attacked, in Italy Vesalius' efforts to revive the Hippocratic tradition were failing, since even Paracelsus was beset by the superstition of the age, as proved by his famous "homunculus" in a bottle.

J. The most ancient Spanish work on syphilis appeared in Venice in 1502, under the title *Libelus de morbo gallico*, written by Juan Almenar of Valencia, who recommended the mercury treatment.

K. Among the writers on syphilis we should mention Francisco López de Villalobos, of Valladolid, who published (Salamanca, 1498) the poem entitled, "Dr. Villalobos on the Contagious and Accursed Buboes"; and Rodrigo Díaz Ruiz de Isla, whose treatise published in 1542 propounded the theory of the American origin of syphilis.

L. "History," said Ortega y Gasset, "is perfect continuity. . . . The historian must seek the origin of any idea arising at any particular date, which is to say, he must look for some other idea arising at some date prior in time."

M. One feature of Valverde's nomenclature, typical of the Renaissance, is the use of numbers in anatomical denominations. The number, which in antiquity was an expression of a magnitude, a length, or a quantity, that is, of something sensorial, measurable, or tactile, became thus something figurative, a symbol of size and rank, a metaphor. The ancient number represented magnitude; the modern number, relation. Ancient anatomists called a particular part of the gut the *duodenum* because it measured the breadth of *twelve* fingers. Valverde used the numerical classification in the muscles in order to denote their mutual relationship.

N. The exact representation of the reality of the form goes hand in hand with the personal interpretation given to it by the artist. When, in Book Three, he wanted to show a pregnant woman, he sketched the rotund shape of a Venus. Artistic inspiration and scientific objectivity knit well together in the illustrational work of Gaspar Becerra.

O. As the *word* is the sensorial expression of a *concept* within whose limits we confine abstract ideas, to name an object, as Valverde did, is to bring it within the ambit of our world, for "through men and numbers, human intelligence gains power over the world," as Spengler said.

P. Valverde incorporated a large number of colloquialisms in his work, thereby establishing them as technical terms—for instance, *tolondrones* (bumps) for condyles, *nudos del espinazo* (spinal knots) for vertebrae, *atajo del pecho* (chest partition) for mediastinum, *tripa ducena* for duodenum, *tripa del cagalar* for rectum—and compared the nerves and their sheaths to the "bark of a tree."

Q. A Galenic test in which the Asiatic or "dry" method was extolled over the Roman or "soft" method with suppuration gave Agüero his inspiration for the dry cure and cicatrization *per primam*.

R. Suárez de Rivera told in the eighteenth century the following story about Valles: "His Majesty Philip II being ill at Badajoz, and in such straits that it was feared he would die within the week, his physicians held a consultation together and Dr. Valles' opinion was contrary to that of the others. The King, however, followed Valles' advice, took the purge he recommended, and was delivered from danger. For having saved his life, the King granted Valles three great honors: first, the title of 'El Divino,' calling him 'my divine Valles'; second, there being no Office of the Royal Physician in a form worthy of Spain, His Majesty entrusted him with the establishment and disposition of such Tribunal; and third, the Divine Valles entering mournfully one day into the presence of the recovered King, His Majesty enquired of him what the matter might be. He replied that there was nothing, but being ordered to answer truly, he obeyed, saying to the King: 'Sire, what hurts me so greatly is that the Admiral (who was present) told me that if your Majesty were to die from taking the purge, he would have to place the rope around my neck.' Upon which the King told the Admiral that men like him came by the dozen but that men like Valles were difficult to come by, since it required extraordinary qualities to become a doctor. At this point, the Admiral devised how to exculpate himself with the King, saying: 'Sire, what I told Valles was that if he did actually cure your Majesty, I would place a rope around his neck, but the rope I had in mind

was the cord of this order of the Golden Fleece, whereof he is more worthy than I am.'" (*Universal Medicine*, by Francisco Suárez de Rivera, Madrid, 1748, pages 37 and 38.)

S. The treatise on "garrotillo" by Nicolás Gutierrez Angulo (1444–1522) is probably the most ancient Spanish work on diphtheria.

T. The first report on spotted fever or endemic typhus came from the New World in Francisco Bravo's *Opera medicinalis* (Mexico, 1560). There were six diphtheria epidemics in Spain from 1581 to 1638, and the disease was first described by Casales, Fontecha, and Villa Real in 1611.

U. During the sixteenth and seventeenth centuries there were epidemic outbreaks of bubonic plague in Barcelona, Seville, Valencia, Saragossa, and Valladolid, all entailing tremendous mortality. They were described by Luis Lucena (1523), Laguna (1542), and Lobera de Avila (1542).

V. See Marti-Ibañez, F.: Three enigmas in the history of curare before Sir Walter Raleigh, Internat. Rec. Med. *164*:700, 1951.

W. Andrés Velázquez in 1585 wrote on melancholy and epilepsy.

X. Other humanists were the Portuguese Amato Lusitano and Isaac Cardoso.

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Chronology of Events in the Time of Don Quixote

1519. Charles I of Spain becomes Holy Roman Emperor (Charles V).

1519-21. Cortez conquers Mexico.

1520. Charles V founds University of Toledo as Colegio de Santa Catalina

1521. Gaspar Torrella publishes *Consilia* on plague epidemic of 1505.

1521-44. Wars between Charles I (Spain) and Francis I (France).

1525. Oviedo describes medicinal plants of New World

1526. Defeat of Francis I at Pavia
Luis Vives publishes treatise on unemployment (*De subventione pauperum*).

1529. Gutierrez de Godoy publishes brief for breast-feeding of infants.

1531-2. Pizarro conquers Peru.

1532. *Constitutio criminalis Carolina* (medical jurisprudence).

1534. University of Sahagún founded as a *studium generale* (later transferred to Irache).

1534-82. University of Huesca.

1535. Andrés Laguna describes the ileocecal valve.

1537. University of Granada founded as Colegio de Santa Cruz (1526).

1539-40. Jesuit order organized.

1540. Luis Vasseo publishes anatomical tables (4) at Paris.

1540-1606. Vittoria (sacred music).

1542. University of Oñate founded.
Ruiz de Isla publishes book on American origin of syphilis.

1542-52. Spanish anatomists theorize about the circulation of the blood.

1544. Lobera de Avila publishes treatise on catarrh, gout, stone, and syphilis.

1545-1625. El Greco

1546. Charles V authorizes publication of first *Index expurgatorius*.

1547. Francesco Borgia, Duke of Gandia, founds University of Gandia (Jesuits).

1547-1616. Cervantes

1548. Andrés Laguna describes method of excising vesicourethral caruncles.

1549. Pedro Gimeno describes the stapes in *Dialogus de re medica*.

1550. Montaña de Monserrate publishes *Anatomia* at Valladolid.

1551. Bishop of Osma founds University of Osma as a *studium generale*.
University of Lima (Peru) founded.
Lobera de Avila publishes first Spanish contribution to pediatrics.

1552. Las Casas publishes account of Spanish cruelty to the Indians.

1553. Viceroy of Peru founds University of Oropesa.
University of Almagro founded (Dominicans).
University of Mexico founded
Servetus describes pulmonary circulation.

1556. Valverde de Hamusco publishes treatise on artistic anatomy.

1556-98. Philip II

1557. Typhus fever (*tabardillo*) appears in Spain.
Juan Huarte completes treatise on vocational aptitude (*Examen de ingenios*), published in 1580.

1558. Charles V renounces crown of Holy Roman Empire.

1562-1635. Lope de Vega.

1564. Francisco de la Reina adumbrates circulation of the blood.

1565. University of Baeza founded.
Porcell describes the plague of Saragossa (1564).

1567-1604. War against the Netherlands.

1568. Archbishop of Valencia founds University of Orihuela (Dominicans).

1569-71. Nicolas Monardes publishes accounts of West Indian materia medica.

1570. Francisco Bravo describes *tabardillo* (Mexican typhus).
Epidemic of sweating sickness in Spain.

1571. Philip II wins naval victory at Lepanto.
Castillian Cortes requires degree of bachelor of astrology as essential to medical degree.

1571-1658. Tirso de Molina.

1572. Archbishop of Tarragona founds University of Tarragona.

1574. Corrella and Toro describe Spanish typhus (*tabardillo*).
Amatus Lusitanus describes valves of azygos vein.

1576. Francisco Arceo publishes book on wound treatment.

1580. Heavy epidemic of influenza in Madrid and Barcelona.

1580-1. Annexation of Portugal.

1583. University of Gerona.
Diphtheria (*garrotillo*) epidemic in Spain.

1584. 6778 students at the University of Salamanca.

1584-5. Luis de Lemos publishes commentary on Hippocratic writings.

1585-6. Smallpox epidemic in Toledo.

1587. Drake burns shipping in the harbor of Cadiz.
Trial and execution of Mary Stuart.

1588. Defeat and wreck of Invincible Armada.
Philip II establishes prescriptive rights of protomedicate.
Arceo's book on wound treatment (1576) translated into English.

1589. Gomez Mendez, Bishop of Albarracin, publishes book on massage.

1590. Acosta describes Andes Mountain sickness.

1594. Luis Mercado publishes book on visceral diseases.

1595. Lopez de Hinojoso publishes surgical treatise in Mexico.

1596. Juan Calvo translates Guy de Chauliac into Spanish.

1598–1700. Period of decadence.

1598–1621. Philip III.

1599. University of Vich founded.

1599–1660. Velázquez.

1600–1681. Calderon de la Barca.

1603. Diphtheria epidemic in Spain.
Rodrigo de Castro publishes treatise on diseases of women.

1604. *Don Quixote* (Part I) published.

1605. University of Oviedo founded.
Daza Chacón publishes surgical treatise.

1608. Luis Mercado describes diphtheria (*garrotillo*).

1609. University of Pamplona founded.

1611. Expulsion of Moors.
Cascales publishes pediatric treatise.
Casales, Fontecha, and Villareal describe diphtheria.

1613. Luis Mercado publishes treatise on diseases of infants.

1614. Velez de Arciniega publishes account of animals useful to medicine.

1615. Rodrigo de Castro publishes book on medical ethics.

1617. Second Part of *Don Quixote* published.
University of Solsona.
Philip III orders re-examination of provincial physicians coming into Madrid (November 7).

1618–48. Thirty Years' War.

1618–82. Murillo.

1619. 32 Universities in Spain.

1620. Bonet publishes book on training deaf-mutes.

Psychopathic Personalities. HAROLD PALMER. New York, Philosophical Library, Inc., 1957. Pp. 179. Price $4.75.

Unfortunately for the reader who picks up this book expecting an exhaustive treatise on that most puzzling and exasperating of psychiatric entities, the psychopathic personality, the title is merely borrowed from the first, and by no means the most comprehensive, essay in a series that covers schizophrenia, depressions, obsession, hysteria, epilepsy, paranoia, and mania as well.

Written informally and not without personal bias, the essays cover most of the variations to be found within the basic types of psychoses as they are generally defined. Those states ordinarily classified as anxiety neuroses are grouped in an essay entitled "The Tension Syndromes." The etiology, course, diagnosis, and treatment of each condition are covered. However, since the author chooses to present his material not visibly supported by research, either of his own or that of others, many of his unqualified statements must be open to question. For example, the statement, "Hysterics are more commonly female than male," may well be disputed on the basis of findings reported by military psychiatrists during World War II and the Korean conflict, which are forcing a revision of this long-held belief.

On the whole, the book, although interesting and readable, presents little that is new, and therefore its value to the psychiatrist, and even to the general practitioner interested in psychiatric problems, is dubious.

An Introduction to Psychopathology. D. RUSSELL DAVIS. London, Oxford University Press, 1957. Pp. 388.

The avowed purpose of this book, in the author's words, is "to build a bridge between the psychiatric clinic and the psychological laboratory," in other words, to provide for psychiatric clinical problems explanations based on the results of psychological testing and experimentation.

To this end the material is gathered and organized, not around clinical entities and the approaches to them of the various schools of psychiatric thought, but around the course of mental growth and development and the disorders of this growth as they appear chronologically. The causative role played by inherited and physical factors is examined through studies of family genetics and environment. Mental disease is divided into disorders of mental development, those of mental function, and those resulting from brain lesions. The chapter on experimental neurosis draws heavily on Pavlov's findings, as has, indeed, all subsequent work in this area, and the experimental work of Masserman with cats is presented. This chapter is amplified by the chapter on applications of behavior theories, which provides explanations for the dynamics of some of the most important symptoms of mental disorder, thereby supplying a rationale for psychotherapeutic methods.

Written by a man who is both a psychiatrist and a clinical psychologist, this book is an interesting and rewarding attempt to explain and reconcile differences

between these disciplines, hitherto often inimical to each other. It will make informative reading for both psychologists and psychiatrists.

Methodology of the Study of Ageing. G. E. W. WOLSTENHOLME AND CECILIA M. O'CONNOR. Boston, Little, Brown & Co., 1957. Pp. 202. 47 illustrations. Price $6.50.

Third in the series of the Ciba Foundation's colloquia on ageing, this volume considers the various techniques for evaluating the physiological and biological aspects of the ageing process. Preceding it were conferences on "General Aspects of Ageing" and "Ageing in Transient Tissues." This book grew out of the desire to examine the many long-term plans for the observation of the ageing process in man and animals now in progress or about to begin in various centers throughout the world.

Included are discussions of the physiological and biological approaches, ageing in cells, measurements of reactions to stimuli at various ages, studies on adaptation, comparative value of studying the whole organism and whole tissue, the use of inbred strains of animals in the study of ageing, the use of twin data on genetics of ageing, problems in methodology in studying changes in human performance, and the methodology of studying intelligence and emotion in ageing.

These papers, and the discussions following them, should stimulate the interest of all those engaged in the relatively new field of gerontology.

Regulation and Mode of Action of Thyroid Hormones. G. E. W. WOLSTENHOLME AND ELAINE C. P. MILLAR. Boston, Little, Brown & Co., 1957. Pp. 311. 114 illustrations. Price $8.50.

This is the first time the Ciba Foundation has devoted an entire symposium to the field of thyroid research, and the results are distinguished. By presenting papers, followed by discussions, from 32 leading investigators, the book attempts to summarize the findings of the last 10 to 15 years, a period during which great advances have been made in the understanding of thyroid function and of the character and mode of action of its hormones. Many differences of opinion are aired, and some resolved.

Among the more provocative of the papers presented are those on the influence of the central nervous system on control of thyrotrophin secretion, hepatic regulation of thyroxine metabolism, influence of the thyroid gland on immune responses of different species to bacterial infection, and the "feed-back" hypothesis of the control of thyroid function. This last is a theory that attempts to provide a working hypothesis of the functioning of the hypothalamic-pituitary-thyroid axis.

The thirty-fourth book in the Ciba Foundation's series, this volume on thyroid function will be of value to all those engaged in research in this field.

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